

# DoD

## Global Emerging Infections Surveillance and Response System



ARMED FORCES INSTITUTE OF PATHOLOGY

MILITARY INFECTIOUS DISEASE RESEARCH PROGRAM

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

UNITED STATES ARMY

UNITED STATES NAVY

UNITED STATES AIR FORCE

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE  
FOR HEALTH AFFAIRS

UNITED STATES REGIONAL UNIFIED COMMANDS

DoD OVERSEAS LABORATORIES

CENTERS FOR DISEASE CONTROL & PREVENTION

UNITED STATES DEPARTMENT OF STATE

PAN AMERICAN HEALTH ORGANIZATION

WORLD HEALTH ORGANIZATION

### ANNUAL REPORT FISCAL YEAR 2006



*Partnering in the Fight Against Emerging Infections*



# DoD Global Emerging Infections Surveillance and Response System

*Partnering in the Fight  
Against Emerging Infections*

Annual Report  
Fiscal Year 2006

Editor-in-Chief	Dr. Luther Lindler
Editorial Director	Lt Col Victor MacIntosh
Editor	Therese Grundl
Executive Editor	COL Ralph Erickson
Section Editors	Dr. Joel Gaydos (Headquarters and Military Health System) LT Jean Paul Chretien (DoD Overseas Laboratories)
Administration	Jennifer Bondarenko, Steve Gubenia
Composition/Printing	Deborah Ford, Henry M. Jackson Foundation for the Advancement of Military Medicine

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#### *Headquarters*

Mario Da Rocha, Dr. Tracy DuVernoy, Jay Mansfield, Robin Miliner, Dr. Richard Miller, Dr. Jose Sanchez, J. Jeremy Sueker, LTC Kelly Vest

#### *Military Health System*

18th MEDCOM Seoul, Korea - LTC Raymond F. Dunton, Jolanta Jacobs, CPT Todd Kijek, Heung-Chul Kim, Dr. Terry Allen Klein, LTC Hee-Choon Lee, Won-Ja Lee, Marie Price, Dr. Leopoldo M. Rueda, COL Martha Sanders, Dr. Richard Wilkerson/ AFIOH San Antonio, TX - Dr. Thomas Cropper, Luke Daum, Matthew C. Johns, Angela Owens, Lt Col Paul Sjoberg/ AFIP Washington, DC - Dr. Victor Kalasinsky, LCDR Lisa Pearce, Dr. Robert Potter, Caroline Wolf/ BAMC Fort Sam Houston, TX - COL Duane Hospenhal, MAJ Clinton K. Murray, MAJ Raven E. Reitstetter, MAJ Timothy Straight, Brenda Torres/ CDHAM Bethesda, MD - Glenn Blanchette/ CHPPM Aberdeen Proving Ground, MD - Nikki N. Jordan, Stephanie Morrison, COL Bruno Petrucci, Kathryn Stamps, MAJ Steven Tobler, MAJ Duvel White/ CHPPM-EUR Landstuhl, Germany - COL Holly Doynce/ CHPPM-West Fort Lewis, WA - Dr. Jim Harrison, Dr. Miguel Quintana, Millie Sola/ LRMC Landstuhl, Germany - LTC Wade K. Aldous, CPT George H. Kallstrom/ NEHC Portsmouth, VA - Gosia Kubiak, CDR Robert Martschinske, Dr. Chris Rennix, Asha Riegodedios/ NEPMU6 Pearl Harbor, HI - CDR Eric Kasowski, LCDR Joseph Sliman, Dr. Scott Thornton/ NEPMU7 Sigonella, Italy - LCDR Ann M. Buff, LT Gary W. Brunette, LCDR Nishith, K. Jobanputra/ NHRC San Diego, CA - LCDR Dennis Faix, Anthony Hawksworth, Marina Irvine, Dr. Pete Kammerer, Dr. Dave Metzgar, Dr. Chris Meyers, Miguel Osuna, CDR Kevin Russell, Jennifer Strickler/ NMRC Silver Spring, MD - Dr. Chien-Chung Chao, Dr. Wei-Mei Ching, Dr. Allen Richards, LCDR Patrick J. Rozmajzl/ OASD(HA) Falls Church, VA - Col Kenneth Cox/ PACAF Hickam AFB, HI - Lt Col Mylene Huynh/ USAMRIID Fort

Detrick, MD - Tamara Clements, Dr. David Kulesh, Dr. David Norwood, MAJ John Michael Scherer, Dr. Randal J. Schoepp, Matthew Voorhees, Dr. Mark Wolcott/ USUHS Bethesda, MD - COL Lisa Keep, LTC Michael Lewis/ DoDVSA Falls Church, VA - LTC Chesley Atchison, COL Gary Vroegindewey/ WRAIR Silver Spring, MD - MAJ Troy Baker, CAPT D.W. Chen, Dr. Desmond Foley, Dr. Dennis Kyle, Dr. Wilbur Milhous, LTC Robert Mott, Dr. Bernards Ogutu, COL Colin Ohrt, LTC Mike O'Neill, Dr. A. Townsend Peterson, MAJ Shon Remich, Dr. Leopoldo M. Rueda, MAJ Norman Waters, Dr. Richard Wilkerson

#### *DoD Overseas Laboratories*

NAMRU-2 Jakarta, Indonesia - LCDR Patrick J. Blair, LCDR Gary Brice, LT Jonathan Glass, CDR Shannon Putnam, CAPT William Rogers, LCDR Craig Stoops/ NAMRU-3 Cairo, Egypt - Dr. Magda Abbassy, CDR Adam Armstrong, CAPT Kenneth Earhart, Dr. Diaa Elyan, COL Raj D. Gupta, Dr. Hanafi Ahmed Hanafi, LCDR David Hoel, Dr. John David Klena, Dr. Moustafa M. Mansour, Dr. Emad Mohareb, LCDR Marshall R. Monteville, Dr. Michael Parker, LCDR Guillermo Pimentel, LT Gregory Racznik, LCDR Mark Riddle, Dr. Atef K. Soliman, Dr. Maha Talaat, MAJ Samuel L. Yingst/ NMRC Lima, Peru - CDR David Blazes, Dr. Jesus Gonzalez, Dr. Carmen C. Mundaca, LCDR Jeff Stancil/ AFRIMS Bangkok, Thailand - LTC Rodney Coldren, LTC Mark Fukuda, Dr. Montip Gettayacamin, LTC Robert V. Gibbons, LTC James W. Jones, LTC Mammen P. Mammen, COL (Ret.) Carl J. Mason, Jr., Dr. Harald Noedl, LTC Bryan Smith, Brian Sweeney/ USAMRU-K Nairobi, Kenya - Dr. Nicholas Adungo, MAJ Sheryl Bedno, Dr. Robert Breiman, Dr. Samson Konongoi, COL Samuel K. Martin, Dr. Jane Mbui, Dr. Kariuki Njenga, Dr. Walter Ochieng, Victor Ofula, Dr. Bernards Ogutu, COL Colin Ohrt, MAJ Shon Remich, MAJ Jason Richardson, Dr. Rosemary Sang, Willie Sang, CPT David Schnabel, MAJ Norman C. Waters/ NASA Greenbelt, MD - Dr. Assaf Anyamba, Piere Formenty, Dr. Kenneth Linthicum, MAJ Sheryl Bedno, Compton J. Tucker, Jennifer Small/ WHO Geneva Switzerland - CAPT Glenn Schnepf

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## Welcome Letter



Greetings from GEIS Headquarters (formerly known as the Central Hub)! It is my great honor to present to you our FY06 Annual Report. In this year, with the provision of the FY06 congressional supplemental appropriation for pandemic and avian influenza, GEIS became a \$50 million enterprise. Here in Maryland we moved into a new facility and hired additional staff, while worldwide we greatly expanded our emerging infectious disease surveillance efforts. Special thanks to all of our partners across our network for making GEIS what it is today and for helping prepare this excellent annual report.

*Ralph Loren Erickson*

Ralph Loren Erickson, COL, MC  
Director, DoD Global Emerging Infections System

## DoD-GEIS Headquarters Staff 2007



*Left to right:* J. Jeremy Sueker, Dr. Richard Miller, Steve Gubenia, Dr. Joel Gaydos, Dr. Tracy Du Vernoy, Mario DaRocha, Robin Miliner, LT Jean-Paul Chretien, Jay Mansfield, LTC Kelly Vest, LtCol Victor MacIntosh, Dr. Jose Sanchez, COL Ralph Erickson, Jennifer Bondarenko, Dr. Luther Lindler.





## Executive Summary

The Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS) was created in 1996 by Presidential Decision Directive NSTC-7, which expanded the role of the DoD to address threats to the United States and other nations posed by emerging and reemerging infectious diseases. In an external review of GEIS five years later in 2001, the Institute of Medicine of the National Academy of Sciences described GEIS as “a critical and unique resource of the United States in the context of global affairs. It is the only U.S. entity that is devoted to infectious diseases globally and that has broad-based laboratory capacities in overseas settings.” A National Intelligence Estimate at that time noted that emerging infectious diseases are a global security issue because they have the capacity to harm US interests abroad through destabilizing key institutions, obstructing trade and human migration, slowing or reversing economic growth, fomenting social unrest, and complicating US response to refugee situations by increasing the demand for humanitarian intervention and through their association with biological terrorism and warfare. The validity of this estimate was supported by the swift appearance of the deadly severe acute respiratory syndrome in 2003 and highly pathogenic avian influenza in 2005.

In FY06, the GEIS Headquarters (formerly known as the Central Hub) coordinated activities with a core budget of \$12 million leveraged through an extensive network of partnerships within DoD and with other US and foreign agencies. In January 2006, GEIS was directed to administer an additional \$39 million in FY06 congressional supplemental funding for avian and pandemic influenza surveillance. With this supplemental funding, GEIS implemented long-term initiatives to increase influenza surveillance, laboratory support, and communication. GEIS priority activities other than influenza were not neglected and continued to advance.

Strengthening the public health capabilities of the DoD overseas laboratories, always a priority of the GEIS mission, continued in FY06. The value of this investment was realized by the capable response of

these laboratories to actual, alleged, and threatening epidemics in support of deployed forces and other populations. Malaria diagnostic resources were improved, and special surveillance programs in Korea provided invaluable information for understanding and combating the troubling reemergence of malaria on the Korean peninsula. Careful monitoring of all possible infectious disease deaths in the US military gained greater efficiency, and diagnostic capabilities for respiratory and other febrile illnesses were enhanced.

The framework of GEIS consists of four goals, of which the first, surveillance and detection, is the primary area of concentration. The three other goals are response and readiness, integration and innovation, and cooperation and capacity building. Each goal encompasses five priority surveillance conditions: respiratory diseases, especially influenza; gastroenteritis syndromes; febrile illness syndromes, especially dengue and malaria; antimicrobial resistance; and sexually transmitted infections. In addition, four broadly based surveillance areas span all emerging infectious disease concerns: mortality surveillance, electronic data capture for surveillance, syndromic surveillance, and modeling.

During FY06, the United States developed its first pandemic influenza plan and helped WHO develop a framework that was largely adopted and integrated worldwide. DoD developed its own plan to be in concert with the US strategy for pandemic influenza. In support of the DoD plan and using core and congressional supplemental funds, GEIS and its partners enhanced influenza laboratory capacity, increased sentinel sites and the number of countries where surveillance is conducted, expanded laboratory diagnostic capability and BSL-3 laboratory capacity, and established centralized communications through the GEIS Headquarters. Significant expansion of laboratory-based capabilities and programs occurred at the Air Force Institute for Operational Health (AFIOH), the Naval Health Research Center (NHRC), and the five DoD overseas research laboratories. All five overseas laboratories now have extensive influenza surveillance programs. The US Army Medical



Research Institute of Infectious Diseases added influenza to its mission and reviewed and developed laboratory tests for agents requiring high containment levels, and the US Army Center for Health Promotion and Preventive Medicine developed methods to provide timely, rapid serosurveillance from serum repository resources as needed. As a result of the expanded mission of GEIS, the Headquarters grew significantly, more than doubling its staff, to meet the need for the enhanced influenza program. To accommodate the new staff, the Headquarters moved into a new facility at 2900 Linden Lane, Silver Spring, Maryland, on 1 October 2006.

A fundamental concern expressed in Presidential Decision Directive NSTC-7 was the continuation of the DoD overseas research laboratories. To address this concern, GEIS has stabilized the overseas laboratories with funding and extensive development of the public health mission of each. NAMRU-3 (Cairo) responded to influenza outbreaks in Iraq and Afghanistan, areas where WHO had little capability; NAMRU-3 has become the WHO influenza reference laboratory for the eastern Mediterranean region and is working in many countries in the Middle East and Central Asia. At NAMRU-2 (Jakarta) and NMRC (Lima), the Early Warning Outbreak Recognition System (EWORS) expanded, facilitating regional networks that will provide early outbreak recognition. AFRIMS (Bangkok) and NMRC, through partnerships with host country militaries and civilian governments, strengthened both military and civilian public health systems in remote areas. The AFRIMS satellite laboratory in Nepal detected and provided advance notice of influenza virus genetic changes that later emerged globally, allowing better vaccine strain selection worldwide. USAMRU-K (Nairobi) initiated influenza surveillance in FY06, making it one of the few laboratories providing reliable data from Sub-Saharan Africa.

GEIS-supported systems and programs responded to many actual, threatening, or alleged epidemics in FY06. In Lima, NMRC continued mosquito surveys to identify, with high resolution, areas at risk for dengue transmission since the disease reemerged there in 2005; risk mapping allowed the ministry of health to target vector control to prevent outbreaks. In Jakarta, NAMRU-2 supported the ministry of health response to an outbreak of

dengue hemorrhagic fever. In September 2006, the GEIS-NASA Rift Valley fever risk prediction project served warning of a possible epidemic in East Africa 2 months before the outbreak began; based on this warning, USAMRU-K deployed a small entomology team to collect specimens in the affected area before the first cases were reported. GEIS also supported large-scale serological surveys in Korea using the DoD Serum Repository to define risk for rickettsial diseases in 10,000 soldiers after deployment to South Korea and in another representative sample of 10,000 active duty forces.

Since 1996, GEIS has directed considerable effort toward improving surveillance systems. GEIS and its partners initiated two automated syndromic surveillance systems: EWORS, which is useful for developing nations, and the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). EWORS, which began in Indonesia, expanded to Cambodia and Lao PDR, and has been established in Peru, employs a methodological approach appropriate for use in countries with a resource-constrained or developmental informatics infrastructure. ESSENCE began as a pilot project in 1999 to provide rapid syndromic morbidity monitoring for 100 DoD clinics in the Washington DC region. As a result of the events of 11 September 2001, ESSENCE was scaled up to encompass more than 300 medical treatment facilities around the world within days. A pioneer in automated syndromic surveillance, ESSENCE helped establish the standards for this new method of surveillance and has been implemented by the state public health authority of Virginia. Its global coverage based on military clinics under surveillance make it a key test bed in evaluating methodologies for data capture, synthesis, analysis, and presentation. ESSENCE is currently an operational system managed by DoD-Health Affairs.

NEHC has used standardized electronic messages from the military laboratory orders to hasten reporting of key infectious diseases and to assist with case finding. In FY06, DoD *Acinetobacter baumannii* case-finding queries supported the outbreak investigation of multidrug-resistant infections in troops from the Iraq theater. When a multi-state outbreak of *Fusarium* eye infections was linked to a commercial ophthalmic solution, cases were identified across DoD in a few hours.

Methods are being developed to estimate difficult-to-measure disease incidence, such as *Chlamydia trachomatis* infections. Pharmacy and radiology data are thought to merit similar evaluation as surveillance data sources; the capture and usefulness of these data are being explored.

Deployment health surveillance data were evaluated through a project sponsored by GEIS and USACHPPM for Operation Enduring Freedom and Operation Iraqi Freedom. Hospitalizations at an Army combat support hospital or air medical evacuations to a EUCOM or CONUS level IV or V treatment facility were tracked. The primary objective was to determine the potential burden of disease and probable risk factors associated with ongoing CENTCOM operations; the secondary goal was to describe in-theater surveillance capabilities. No single system was found to provide reliable, timely, and complete data; however, improvements were demonstrated with the combined analysis of the available data from multiple systems.

Near real-time global mortality surveillance is conducted by the Armed Forces Institute of Pathology in the Office of the Armed Forces Medical Examiner. Work begun through GEIS has led to improvements in all active duty mortality data collection. Of particular importance is the strengthened collaboration between the Armed Forces Institute of Pathology and NHRC in the laboratory investigation of deaths from respiratory infection. The death of an otherwise healthy servicemember from an infectious disease serves as an important sentinel event for all emerging infectious diseases, particularly pandemic influenza.

GEIS partners made crucial contributions to surveillance for malaria in FY06. An international Malaria Diagnostic Center of Excellence was established in Kisumu, Kenya, by the WRAIR Division of Experimental Therapeutics in collaboration with USAMRU-K and the Kenya Medical Research Institute to improve microscopy accuracy in surveillance, research, and clinical programs. Through this program, more than 200 microscopists from 11 countries have been trained, and significant improvements in performance were achieved. The DoD overseas laboratories continue to monitor antimalarial drug resistance, supplementing

ministry of health and WHO efforts with sophisticated laboratory methods. Critical overseas laboratory surveillance in Southeast Asia, where anti-malarial drug resistance has emerged, is monitoring early indications of artemisinin resistance because these drugs are deployed widely throughout the region. Mosquito collections by 18th MEDCOM (Korea) linked with molecular analysis and modeling at the Walter Reed Biosystematics Unit have precisely identified the species involved in malaria transmission and the reemergence of malaria in Korea in the vicinity of the Demilitarized Zone.

In the area of infectious disease modeling, GEIS brought together experts in the field for a conference in August 2005 and followed with discussions in FY06. The result was the initiation of two significant projects. First, influenza infection, transmission, and spread have not been adequately described in contemporary military recruits at initial entry training sites. In partnership with the Johns Hopkins University Applied Physics Laboratory, GEIS initiated a study in which significant variables are identified through modeling; this project should lead to identification of interventions and control strategies, the effects of which can be modeled and measured in advance of an influenza pandemic. Another significant effort using the same partnership is examining influenza in an overseas civilian population. This latter effort has provided a unique opportunity to evaluate EWORS. Second, NHRC is monitoring influenza vaccine failures in military recruits. For the third consecutive year, NHRC used recruit respiratory surveillance data, combined with modeling, to provide estimates of US seasonal influenza vaccine effectiveness.

Currently GEIS is the only robust, well-developed system within the US government with a mission of health surveillance through the monitoring of infectious disease outbreaks using syndromic and diagnostic methodologies. GEIS programs continue to identify and address critical gaps in emerging infectious disease preparedness. Through its accomplishments and capabilities, GEIS continues to contribute to force health protection and is a vital partner in the global effort to identify and control emerging infectious diseases.

# Introduction

From the battlefield to the training installation, force health protection is a complex multifaceted endeavor that must be integrated to achieve and maintain the highest possible state of operational readiness for the armed forces. Combat-related injuries historically receive much of the attention from inside and outside the military. However, non-combat-related injuries, specifically disease nonbattle injuries, cause the most casualties in the military and therefore severely affect force readiness (Figure 1).

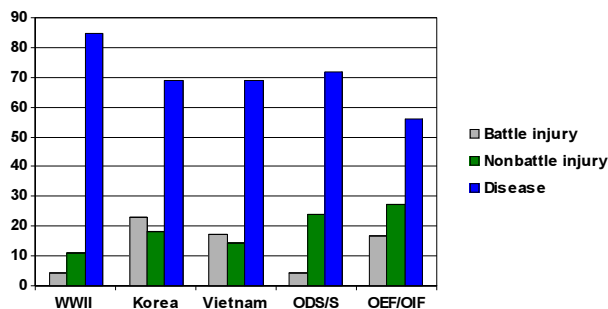


Figure 1. Percent of hospitalizations in US military caused by battle injury, nonbattle injury, and disease in wars and conflicts since World War II (WWII). ODS/S, Operation Desert Storm/Shield; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom.

This fact has been true for every conflict or war in which the United States has been involved and continues today. In Operation Iraqi Freedom there have been six times as many non-combat-related aeromedical evacuations compared with combat-related evacuations.<sup>1</sup> A 2005 survey of Operation Iraqi Freedom and Operation Enduring Freedom veterans found that more than 10 % had missed at least one patrol or one air operation because of illness.<sup>2</sup> According to the same survey, the most common diseases in Operation Iraqi Freedom were diarrhea and respiratory illnesses, with 77 % and 69 % of respondents, respectively, having experienced at least one episode during their deployment. Approximately one-quarter of the respondents stated that these infectious diseases had negatively

impacted unit operational effectiveness.<sup>2</sup> Respiratory infectious diseases account for 25–30 % of military hospitalizations, and disease rates in trainees exceed those in similarly aged civilian populations.<sup>3</sup> Infectious diseases significantly affect training, operations, and operational readiness in all military forces.

Infectious diseases occurring in overseas civilian populations can also threaten US security. Epidemics can spread in areas with poor public health infrastructure and directly involve US forces or civilians or can cause social, political, and economic disruption. The severe acute respiratory syndrome (SARS) epidemic of 2003 demonstrated how fast a previously unknown disease can emerge and spread. After spending one night in a Hong Kong hotel on the same floor as a physician who was infected while caring for SARS patients in China, hotel guests carried the disease directly to Canada, Vietnam, and Singapore. The epidemic eventually infected more than 8,000 people in 26 countries and cost the global economy around \$40 billion. As of late 2006, with highly pathogenic avian influenza (H5N1) endemic in parts of Asia and several episodes of limited human-to-human transmission, public health leaders around the world are preparing for an influenza pandemic. Should a pandemic occur, the consequences to US security and economic interests could be enormous. Effective surveillance of overseas civilian populations provides a framework for early warning of newly emerging diseases and provides the local US military commanders with infectious disease situational awareness.

The mission of the DoD Global Emerging Infections Surveillance and Response System (DoD-GEIS) is to serve force health protection by countering the largest threat to the health of the force, infectious diseases. DoD-GEIS conducts surveillance and response for emerging infectious diseases within the military and in foreign civilian populations through

<sup>1</sup> Harman DR, Hooper TI, Gackstetter GD. Aeromedical evacuations from Operation Iraqi Freedom: a descriptive study. *Mil Med* 2005;170(6):521-7.

<sup>2</sup> Sanders JW, Putnam SD, Frankart C, et al. Impact of illness and non-combat injury during Operations Iraqi Freedom and Enduring Freedom (Afghanistan). *Am J Trop Med Hyg* 2005;73(4):713-9.

<sup>3</sup> Gray GC, Callahan JD, Hawksworth AW, Fisher CA, Gaydos JC. Respiratory diseases among U.S. military personnel: countering emerging threats. *Emerg Infect Dis* 1999;5(3):379-85.

the long-standing DoD overseas medical research laboratories. GEIS focuses on diseases that threaten US forces and their families, including newly appearing infectious agents or well-known agents that are increasing in incidence or geographic range.

The GEIS strategic plan is based on the following four goals:

- Surveillance and detection
- Response and readiness
- Integration and innovation
- Cooperation and capacity building

These four goals form the pillars of GEIS and give it the ability to recognize and identify emerging diseases, either in training or deployed forces, that pose a threat to readiness. Although GEIS monitors all infectious diseases in military forces, the following are priority surveillance conditions:

- Respiratory diseases, especially influenza
- Gastroenteritis syndromes
- Febrile illness syndromes, especially dengue and malaria
- Antimicrobial resistance
- Sexually transmitted infections

Since its founding in 1996, GEIS has addressed these conditions, particularly respiratory diseases and febrile illness. In FY06 GEIS received congressional supplemental funding for pandemic and avian influenza, which represented a five-fold increase in the annual GEIS budget, specifically for monitoring and responding to the threat of pandemic and avian influenza. This supplemental funding, received in March 2006, was part of the overall DoD Implementation Plan for Pandemic Influenza, action item 4.2.3.8. GEIS was tasked with enhancement of influenza surveillance efforts through its network of the five DoD overseas laboratories.

The enhancement of the GEIS influenza surveillance network to help the United States prepare for pandemic influenza took advantage of one of the greatest successes of GEIS: the consistent investment to develop both laboratory diagnostic surveillance and syndromic surveillance efforts, especially for

influenza. The hub of the GEIS diagnostic effort for influenza is located at the AFIOH. AFIOH is also an official WHO collaborating laboratory. The NHRC is the primary DoD laboratory for respiratory illness, especially in trainees, and is partially supported by GEIS. Together, AFIOH and NHRC are the GEIS reference laboratories for influenza laboratory diagnosis and surveillance. AFIOH conducts surveillance for influenza-like illness among military personnel and dependents, the data for which are gathered principally from reporting military treatment facilities worldwide. In contrast, NHRC primarily monitors recruit training sites, shipboard personnel, and Mexican border populations for febrile respiratory illness. NHRC regularly exchanges information and results with AFIOH, which then shares information with the CDC influenza program.

The five DoD overseas laboratories are essential to the GEIS influenza surveillance network. Figure 2 illustrates areas throughout the world that have reported highly pathogenic avian influenza H5N1 in birds and the positioning of influenza surveillance sites. Of particular interest for influenza is NAMRU-2 in Jakarta. Indonesia is in one of the world's most concerning hot spots for avian and pandemic influenza because of the increasing number of human avian influenza cases there and the increased mortality compared with other countries reporting this disease. As of late 2006, Indonesia reported the second highest number of human cases of H5N1 infection in Asia. NAMRU-2 provides significant capability and capacity to support the Indonesian Ministry of Health and the WHO.

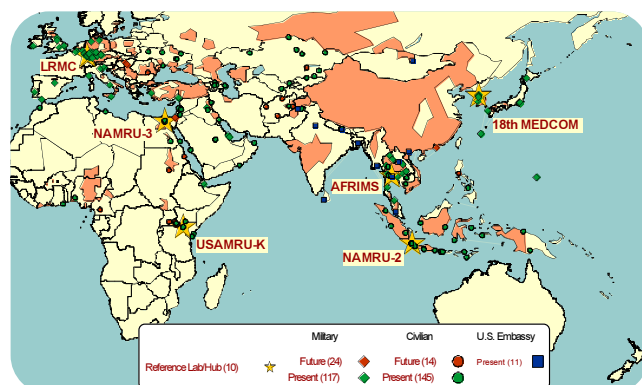


Figure 2. Areas of documented influenza A/H5N1 infections in birds (pink) in relation to DoD influenza surveillance sites and overseas laboratory assets. Blue boxes, US embassies that send influenza-like illness specimens to DoD overseas laboratories for analysis (WHO, November 2006).



The DoD overseas laboratory in Cairo, NAMRU-3, has performed influenza surveillance in several countries within the CENTCOM area of responsibility, including animal studies in Iraq and human surveillance in Afghanistan and Egypt. This is fitting since Egypt has reported the fifth largest number of avian influenza cases in humans worldwide.

In Bangkok, the AFRIMS overseas laboratory joins NAMRU-2 at the center of concern about avian and pandemic influenza, given that Thailand has reported the third largest number of human cases of H5N1 infection globally. A recent article in the *Proceedings of the National Academy of Sciences*, which details the behavior of the highly pathogenic avian influenza H5N1 in China, confirms the value of the GEIS surveillance by stating that despite the achievements of the Chinese surveillance network, “...there remains a lack of information in the broader region and it is critical that similar surveillance programs begin in other areas, including Indonesia, Vietnam, Thailand and India.”<sup>4</sup> GEIS is uniquely positioned to fill this need with its established and growing surveillance network including NAMRU-2, AFRIMS, and NAMRU-3.

Although influenza has always been fundamental to DoD-GEIS programs, GEIS continues to monitor and respond to other emerging infections. Figure 3 shows outbreaks of infectious diseases that occurred in FY06 that were investigated by GEIS partners. GEIS programs are in accordance with a recent analysis of preparations for emerging infections by the forward-looking Foresight Program.<sup>5</sup> Funding and effort have been invested by GEIS in six of the eight categories of infectious diseases of the future identified by the Foresight Program. These infectious diseases include highly pathogenic influenza H5N1, antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, zoonoses,

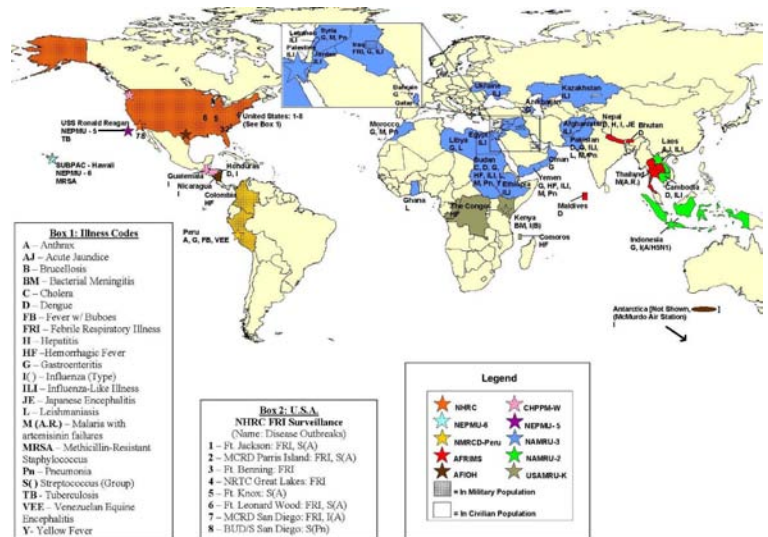


Figure 3. Outbreak investigations conducted by GEIS partners in FY06, most of which were funded by GEIS. Box 1 shows disease outbreaks investigated by NHRC in recruit training centers inside the United States.

malaria, acute respiratory illness, and sexually transmitted infections. The two categories identified in the report in which GEIS has not invested are infectious agents that target plants or animals.

GEIS programs are focused on emerging infectious disease threats to US forces and other DoD health care beneficiaries around the world. The Headquarters coordinates the activities of the funded projects, including those at the overseas laboratories, to provide the military health system with subject matter expertise in epidemiology, public health/preventive medicine, infectious disease, as well as laboratory diagnostic testing and to provide timely infectious disease surveillance information to the GEIS partners. In many areas of the world, the only available surveillance data are provided by GEIS-funded programs. Thus, GEIS efforts benefit not only the DoD but the entire US and global health communities.

Currently, GEIS is organized in two divisions: the Influenza and Zoonotic Diseases section and the Epidemiology and Military Health Systems section. Of note, a new GEIS communication center was

<sup>4</sup> Smith GJ, Fan XH, Wang J, et al. Emergence and predominance of an H5N1 influenza variant in China. *Proc Natl Acad Sci U S A* 2006;103(45):16936-41.

<sup>5</sup> King DA, Peckham C, Waage JK, Brownlie J, Woolhouse ME. Epidemiology. Infectious diseases: preparing for the future. *Science* 2006;313(5792):1392-3.

recently established and will serve to coordinate communications for GEIS and the future Armed Forces Health Surveillance Center (AFHSC) as it relates to emerging infectious diseases. GEIS, along with the Army Medical Surveillance Activity at USACHPPM will form the major divisions of the future AFHSC in mid-2007 and beyond and will respond directly to the Assistant Secretary of Defense for Health Affairs.

Among the strengths of GEIS are the availability of funds and the professional expertise to apply those funds toward identified problem areas in the MHS. The development of programs and projects related to infectious disease in this manner ultimately increases operational readiness by promoting force health protection. GEIS surveillance projects in the overseas and military reference laboratories provide actionable and timely information to the MHS and COCOMs and advance the development of emerging technologies for system integration to identify potential biothreats before they occur. GEIS supports response and readiness through the funding of rapid response and train-the-trainer workshops as well as professional workshops and tabletop exercises related to specific infectious disease issues.

Reports of FY06 GEIS activities at the Headquarters, throughout the MHS, and at the DoD overseas laboratories are presented in this report. Selected accomplishments that GEIS is particularly delighted to present follow:

- Expanded influenza surveillance from 30 to 56 countries, with significant increases in the Middle East, Africa, and Southeast Asia;
- Increased influenza diagnostic capacity from 9,000 specimens per year in FY05 to 18,000;
- Increased number of DoD-associated high containment biosafety level 3 facilities to four, with an expected increase to eight in FY07 that will include regional capabilities in Korea, Europe, South America, and Southeast Asia;
- Integration of health surveillance and report data with establishment of a GEIS communications center to become an integral part of the AFHSC in FY07;

- Enhanced capability of DoD influenza reference centers to identify influenza A subtypes to foster early identification of potential pandemic strains;
- Support for DoD actions in the areas of homeland security and force health protection through the establishment of Mexican border febrile respiratory illness surveillance and diagnostic testing and through development of an interactive relationship among the Headquarters, the National Biosurveillance Integration Group, and NORTHCOM;
- End-to-end analysis of DoD-wide capabilities to perform influenza diagnostic testing, conducted and reported through the Headquarters;
- Development of integrated team within the overseas laboratories, Headquarters, and the Johns Hopkins University Applied Physics Laboratory to further develop capabilities within the Early Warning Outbreak Recognition System for syndromic surveillance;
- Key role in design, scientific review, and data monitoring of a large, Phase III clinical efficacy trial of adenovirus 4 and 7 vaccines among military recruits at Fort Jackson (South Carolina) and Great Lakes Naval Training Center (Illinois);
- Sponsorship of workshop entitled “Emerging Infectious Disease Modeling: Epidemiologic Applications in the Department of Defense,” the proceedings of which were published in the January 2006 issue of *Emerging Infectious Diseases*; fundamental aspects of pandemic and avian influenza and emerging infectious disease modeling were addressed, and the need for further expansion of these efforts within DoD was indicated;
- Development of the NASA project for the identification of environmental conditions that could favor disease outbreaks; this satellite-based effort provided an alert of Rift Valley fever risk in East Africa 2 months before an epidemic began in late 2006, facilitating deployment of a field team from USAMRU-K before cases were reported;
- Pandemic and avian influenza preparedness and response training workshops with the Pacific Air Forces and DoD Veterinary Service Activity that enhanced rapid response capabilities of US government and foreign militaries and ministries of health by integrating public health systems surveillance and response in countries at high risk of pandemic influenza emergence.



# Headquarters

## Congressional Supplemental Funding for Pandemic and Avian Influenza

Considerable Headquarters (formerly known as the Central Hub) effort was directed toward the FY06 congressional supplemental funding for pandemic and avian influenza. A comprehensive military influenza surveillance center was established within the Headquarters to develop, implement, and coordinate this initiative. The influenza surveillance center stood up in May–June 2006 and was integrated into the existing GEIS global network. A coordination office within the military influenza surveillance center was established to support a unified DoD effort for gathering and assessing information from influenza and other respiratory disease surveillance and identifying situations that could threaten the health and operational effectiveness of military personnel, the health of other DoD health care beneficiaries (e.g., dependents), and efficient, informed corporate decision-making.

The Headquarters staff was also intimately involved with the writing of a DoD implementation plan for pandemic and avian influenza emergency preparedness and response. Critical to this effort was the establishment of a communications center within the Headquarters to monitor avian and seasonal influenza activities among GEIS partners and other agencies. Additionally, a GEIS-specific pandemic and avian influenza strategic plan and a concept of operations document to define the role and activities of the communications center were developed.

As part of the pandemic and avian influenza emergency preparedness plan, the Headquarters coordinated surveillance and epidemiologic investigation efforts with the Army Medical Surveillance Activity (USACHPPM) and the Deployment Health Support Directorate (Office of the Assistant Secretary of Defense for Health Affairs) and hired a full-time GEIS coordinator for the 18th MEDCOM Force Health Protection Office in Seoul, Korea.

Four professional meetings and tabletop exercises that emphasized avian and pandemic influenza preparedness were supported by the Headquarters during FY06:

- Army National Guard medical team conference in Dallas in May 2006, attended by 180 registered participants representing 53 of 54 states and territories;
- USACHPPM-sponsored Force Health Protection conference in Albuquerque, New Mexico, in August 2006, attended by 1,694 participants;
- Avian influenza training conference and surveillance workshop in Washington DC in August 2006 in support of the Army's Office of the Surgeon General and the DoD Veterinary Services Activity, attended by 62 participants;
- Pandemic influenza preparedness tabletop exercise at Fort Myer, Virginia, in September 2006, attended by more than 100 representatives of military and civilian organizations in the Washington DC area.

Effective surveillance, which is essential for pandemic influenza detection and containment, faces challenges in developing countries such as those currently affected by influenza A/H5N1 (highly pathogenic avian influenza virus). To identify successful strategies for early warning systems in developing countries, the Headquarters initiated collaboration between GEIS and the Johns Hopkins University Applied Physics Laboratory (JHU/APL; Baltimore, MD). Two modeling projects were developed to improve GEIS surveillance and response systems.

The first is a quantitative and qualitative evaluation of the Early Warning Outbreak Recognition System (EWORS), a syndromic outbreak detection system developed in 1998 by NAMRU-2 (Jakarta, Indonesia). EWORS now operates in three south-east Asian countries and Peru. The project team, which included scientists from JHU/APL, NAMRU-2, NMRC (Lima, Peru), and the Headquarters, focused on the EWORS network in

Lao PDR that was implemented in 2003. The team was privileged to receive the full support, encouragement, and interest of the Lao Ministry of Health. The modeling was based on demographic and health data provided by the Ministry of Health, comprehensive EWORS data on respiratory disease presentations since EWORS was implemented in Lao PDR, and on-site evaluations of EWORS operations in Vientiane and Luang Prabang. Preliminary recommendations have been provided to the Ministry of Health; a detailed influenza transmission and surveillance and response model for quantitative EWORS evaluation is being developed. Statistical, technological, and training enhancements are being explored that may apply to other EWORS locations and early warning surveillance systems in resource-poor settings.

The second JHU/APL modeling project is based on pandemic influenza transmission, detection, and containment in recruit training environments where the risk of respiratory disease outbreaks is high and where previous novel influenza strains have caused epidemics. Data for the model are from Fort Leonard Wood (Missouri) and were collected during JHU/APL site visits and through an extensive literature review using a hybrid agent- and population-based approach. Software is being developed to allow DoD public health decision-makers at facility and higher levels to evaluate surveillance and containment strategies. The basic model is being extended to other military scenarios, such as installations that are undergoing large-scale mobilization or demobilization operations and that are within or near large metropolitan areas.

In late FY06, the Headquarters initiated an independent external review of GEIS to be conducted by the Institute of Medicine to evaluate the FY06 and FY07 influenza surveillance and response efforts supported through GEIS funding. The goal is to provide a credible, expert evaluation of GEIS accomplishments, to provide advice about improving surveillance and response efforts, and to recommend subsequent efforts that could be undertaken to enhance the likelihood of early detection and timely response to an influenza pandemic.

## Prevention of Respiratory Disease in Military Populations

Respiratory diseases are a major cause of morbidity in the US military. The Headquarters supports the AFIOH as the central laboratory of the DoD Global Influenza Surveillance Program and the NHRC as the central laboratory for febrile respiratory illness surveillance in military trainees. These centers foster cooperation among the GEIS partners as well as among other DoD organizations, the CDC, and the WHO. The Headquarters staff continued to serve as consultants and sources of information to support studies of acute, febrile, respiratory diseases of military importance and to facilitate information exchange. In FY06, the Headquarters assisted GEIS partners with the development, conduct, and completion of surveillance, laboratory, and clinical trial projects and programs, such as the DoD Phase III adenovirus vaccine trials at Fort Jackson (South Carolina) and the Great Lakes Naval Training Center (Illinois).

## Sexually Transmitted Infections

Sexually transmitted infections are costly, and sequelae such as pelvic inflammatory disease, chronic pelvic pain, and infertility can significantly diminish quality of life and adversely affect military readiness. GEIS initiatives continued to direct attention to the importance of sexually transmitted infections in the military. The Headquarters was a resource for information on sexually transmitted diseases and sexually transmitted infections in Military Health System beneficiaries. Information and professional assistance were provided on request to DoD medical personnel, including the DoD overseas laboratories and Armed Forces Epidemiological Board members. At the request of the Fort Knox (Kentucky) preventive medicine physician, the Headquarters provided professional assistance and coordination, with Johns Hopkins University, in the development and evaluation of an initiative for *Chlamydia trachomatis* screening. Fort Knox, Johns Hopkins University, and GEIS personnel also collaborated with the Army Medical Surveillance Activity in the development of a model for assessing the cost-effectiveness of screening male recruits for *C. trachomatis*. At the request of the Armed Forces Epidemiological Board (AFEB) president, the Headquarters coordinated a review of

## GEIS Surveillance for Influenza

The principal goal of the triservice GEIS is to coordinate in the DoD the establishment and maintenance of surveillance for, detection of, and response to emerging infections that threaten military populations. Overall, this system is an important source of global information regarding the status of influenza and its impact on US military and civilian populations worldwide.

GEIS surveillance is laboratory-based, consisting of a comprehensive network of military and civilian health facilities, overseas research laboratories, and field sites that were significantly enhanced during FY06. Influenza specimens are now accrued from approximately 273 participating sites in 56 countries and many large-deck ships of the US Navy; 38 sites in nine countries are to be added in FY07. Many sites are located in regions of the world where DoD has the only existing laboratory-based surveillance capacity.

The GEIS influenza surveillance system comprises three components:

1. Sentinel surveillance among military and dependent personnel in the United States and overseas;
2. Population-based surveillance among recruits undergoing initial entry training, shipboard personnel deployed to geographically dispersed regions of the world, and populations along the Mexican border;
3. International surveillance of local populations in five far-reaching regions outside the United States.

**Sentinel surveillance within military.** Approximately 9.2 million medical beneficiaries are monitored, including 2.4 million active duty and reserve personnel and 120,000 health care workers distributed worldwide. To address the medical beneficiaries, sentinel surveillance for influenza-like illnesses among military and dependent populations is routinely conducted by the AFIOH. More than 60 sentinel military MTFs in the United States, Europe, Japan, and Korea are included as well as many deployed and field units in the CENTCOM area of responsibility.

**Population-based surveillance.** NHRC routinely monitors recruits at eight US initial entry training centers; deployed shipboard populations in the 3rd Fleet (eastern Pacific), 2nd Fleet (Atlantic), and 7th Fleet (western Pacific); and patients at two clinics on the Mexican border for febrile respiratory illnesses.

**International surveillance.** Surveillance of host nation civilian and military populations is managed largely by the five DoD overseas research laboratories located in Egypt, Indonesia, Kenya, Peru, and Thailand. These efforts augment the global influenza surveillance work of WHO. Through this robust, unique global surveillance work within DoD, during the past 7 years, DoD has made contributions leading to four key influenza A subtypes being incorporated into the seasonal influenza vaccine.

DoD shares influenza specimens with the CDC as well as WHO; isolate subtyping and genetic sequencing data are also shared. Since 1998, the CDC has received more than 900 influenza isolates from AFIOH.

The DoD-GEIS network plays a significant role in the global monitoring of influenza and other emerging infectious diseases. Its US-based laboratories and forward-deployed laboratory platforms serve as a unique and essential monitoring system to detect emerging pathogens, particularly pandemic influenza virus. The diversity of the influenza isolates obtained through GEIS global surveillance helps to identify disease trends and changes in virus strain composition worldwide. These data are vital to the development of effective seasonal and pandemic influenza vaccines.



Unique DoD assets that comprise DoD global network for influenza surveillance.

chlamydia screening in the DoD for the AFEB meeting in San Diego in December 2004. In collaboration with USACHPPM, selected aspects of the presentation to the AFEB were updated and expanded, and the results of this effort was presented at a peer-reviewed international sexually transmitted infection meeting in June 2006 in Niagara-on-the-Lake, Ontario, Canada.

### Antimicrobial Resistance (TSN/Antimicrobial Resistance Task Force)

Recognizing the threat of antimicrobial resistance, GEIS has encouraged the development of a DoD-wide surveillance mechanism for identifying antimicrobial resistance occurrences and trends. Through a cooperative agreement with Focus Bio-Inova (Herndon, VA), four military medical centers participate in the world's largest electronic database and surveillance system for antimicrobial resistance, The Surveillance Network (TSN).

An interagency task force on antimicrobial resistance was formed in 1999 and is co-chaired by the CDC, Food and Drug Administration, and the National Institutes of Health and includes representatives from the DoD, Veterans Affairs, Department of Agriculture, Environmental Protection Agency, and other organizations. The task force developed a public health action plan to combat antimicrobial resistance. Part I, published in 2001, focused on domestic issues. An overarching goal is a coordinated national surveillance plan, including reliable drug susceptibility data from clinical sources and the ability to monitor antibiotic drug use. Part II will address global collaborations. The Headquarters has provided DoD representation to the task force since its formation and continues to review and update a DoD inventory of projects and activities (e.g., TSN and outbreak investigations) that is included in the published annual reports of the task force.

### Epi-X

The CDC Epidemic Information Exchange (Epi-X) is a secure, web-based communications network

that serves as a communications exchange between CDC, state and local health departments, poison control centers, and other public health professionals, including representatives from other nations (e.g., Canada and Mexico). The system provides rapid reporting and immediate notification. Only public health officials designated by their agency may participate in Epi-X. The GEIS Headquarters has encouraged DoD participation in Epi-X for several years. In FY06 GEIS cosponsored training for military users, had representation on the Epi-X editorial board, and consulted with CDC and DoD staff members to coordinate the use of Epi-X by the DoD. Currently, more than 90 DoD personnel representing a wide variety of organizations at installation, major command, service, agency, and other levels use Epi-X. CDC officials cite regular reports from the DoD Global Influenza Surveillance Program (AFIOH/GEIS), the febrile respiratory illness surveillance program (NHRC/GEIS), and outbreak reports, such as tuberculosis exposure aboard the aircraft carrier USS *Ronald Reagan* (NEHC/NEPMU-5),<sup>1</sup> as major contributions by DoD.

### Professional Meetings

In FY06 the Headquarters supported several professional meetings. Selected examples follow: International Conference on Emerging Infectious Diseases (Atlanta, GA), Force Health Protection Conference (Albuquerque, NM), Army National Guard medical team seminar (Dallas, TX), EWORS symposium in December 2005 at WRAIR (Silver Spring, MD), and American Society of Tropical Medicine and Hygiene symposium in Washington DC. In addition to delivering peer-reviewed presentations, GEIS support included participation on program planning committees, critical review of submitted abstracts, provision of speakers for invited presentations and session moderators, and administrative and financial assistance. In addition, the report of a GEIS-sponsored workshop entitled "Emerging Infectious Disease Modeling: Epidemiologic Applications in the Department of Defense," held on 3 August 2005 at WRAIR, was completed and published in a peer-reviewed journal.

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<sup>1</sup> CDC. Brief report: Latent tuberculosis infection among sailors and civilians aboard the USS *Ronald Reagan*-United States, January–July 2006. *Morbidity and Mortality Weekly Report* 2007;55:1381–1382.



The Headquarters arranged and regularly conducted DoD-wide telephone conference calls, the epidemiology chiefs' biweekly teleconference (epi-chiefs). The objective of these calls is to exchange information on infectious disease threats among people in key military positions and others, such as the DoD liaison officer at the CDC (Atlanta, GA).

Teleconferences lasted one hour, and each involved 20 or more participants from AFMIC, AFIP, AFIOH, SOUTHCOM, NORTHCOM, POPM, USACHPPM, WRAIR, NEHC, NHRC, CDC, and DoD-Health Affairs; 24 epi-chiefs teleconferences were held in FY06. Regular agenda items included outbreaks, recent mortalities, respiratory disease incidence, influenza incidence, other febrile illness incidence, and a roundtable of open discussion. Among the benefits of these teleconferences are the provision of current information; the stimulation of productive interactions, e.g., the treatment of malaria caused by drug-resistant *Plasmodium vivax* in Operation Enduring Freedom returnees and the issue of Q fever in forces deployed in Operation Iraqi Freedom and Operation Enduring Freedom; and the provision of assistance when needed, e.g., the identification of laboratories that could provide special testing. The proceedings of the epi-chiefs meetings were transcribed, and the transcriptions and summaries were reviewed by participants before distribution to a larger DoD-wide audience. Teleconference summary information was also placed on the GEIS secure website for reference and as a resource.

Since DoD-GEIS was founded in 1996, DoD and CDC personnel have strived to exchange information, coordinate projects and programs, share common priorities, and avoid duplication. With an increasing number of new initiatives, projects, and programs, DoD and Department of Health and Human Services (HHS) leaders called for a structured, periodic telephone or video conference

of key DoD and CDC/HHS personnel to ensure cooperation and collaboration in government efforts in response to the threat of pandemic and avian influenza and to avoid duplication in all areas of emerging infectious disease interest, particularly overseas. These conferences began in January 2006 as a DoD-CDC/HHS working group, for which the Headquarters assumed administrative responsibility. In FY06, four teleconferences and one face-to-face meeting took place. Typically 12–14 individuals from HHS, CDC, DoD-Health Affairs, GEIS, AFIOH, NHRC, and the DoD overseas laboratories participated. These interactions improved understanding of each organization's plans, priorities, and funding for OCONUS surveillance.

## Mentoring

Education and training in emerging infections are essential to the GEIS pillar of capacity building. The Headquarters provides mentoring to fellows, resident physicians, graduate students, and medical students who have interest in emerging infections of military importance. The Headquarters identifies potential projects for fellows, residents, or students and communicates this information to the faculties of the Uniformed Services University of the Health Sciences (Bethesda, MD), WRAIR, and other academic institutions. Alternatively, faculty advisors of trainees in military or civilian institutions may contact the Headquarters with proposed projects or offers to collaborate. Mentoring may occur formally for long-term projects or informally for addressing single issues or current topics. In FY06, mentoring was provided by the Headquarters for four individuals: two resident physician projects, one graduate student project, and an extensive program for a Harry S. Truman Foundation Scholar.

# Military Health System

## *Air Force Institute for Operational Health*

The Air Force Institute for Operational Health (AFIOH; Brooks City-Base, TX) forms the backbone of GEIS surveillance for influenza and directly supports laboratory-based surveillance for DoD sentinel sites worldwide, outbreak investigations, and the activities of USACHPPM-West and the overseas laboratories in Lima and Bangkok. (Other DoD influenza surveillance activities overseas interact directly with the CDC or another WHO Collaborating Centre for influenza.) In conjunction with the Joint Influenza Surveillance Working Group, a professional network of DoD programs involved in influenza surveillance that meets annually to review progress and plan future efforts, AFIOH has annually expanded its geographic presence and participation in the DoD influenza surveillance program since 1997, when DoD designated the Air Force as the executive agent for influenza surveillance. The experience of the Air Force with influenza work extends to 1976, when an influenza surveillance system called Project Gargle was initiated at key Air Force installations worldwide. GEIS work at AFIOH is guided by the Health Affairs Policy Memo 99-08<sup>1</sup> and the DoD Implementation Plan for Pandemic Influenza.<sup>2</sup> Accomplishments during the 2005–2006 influenza season have continued to improve the effectiveness of surveillance efforts at DoD sentinel sites.

### Surveillance

GEIS and AFIOH surveillance efforts expanded this season as established working relationships increased dramatically from 34 to 65 DoD sentinel sites in 34 countries (43 military sites and 22 nonmilitary collaborating sites in host nations). A total of 50 of the 65 sentinel sites actively participated by submitting specimens in FY06. In

addition, USAMRU-K, the DoD overseas laboratory in Nairobi, and USACHPPM-West personnel working with Joint Task Force-Bravo (JTF-Bravo) medical representatives and local health officials in Honduras began routine participation in the AFIOH influenza surveillance program. The extent of DoD global surveillance for influenza is illustrated in Figure 4.

AFIOH provided staff-specific educational materials for support to all sentinel sites before the beginning of the season. Materials included a program brochure, an educational presentation,

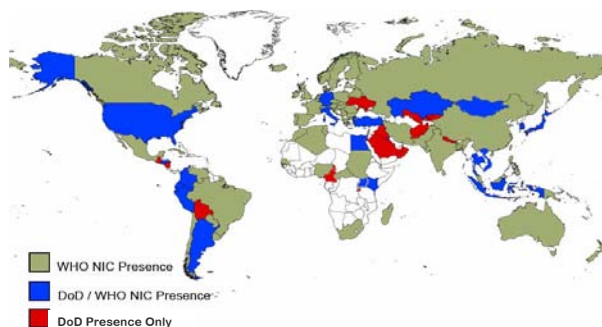


Figure 4. Areas covered by DoD influenza surveillance, showing global reach achieved with sites added by AFIOH in FY06. NIC, National Influenza Center.

staff-specific educational pamphlets, a one-page guidance sheet, specimen collection kits, and influenza surveillance questionnaires. This educational effort increased awareness and led to over 90 % of the sentinel sites completing the invaluable questionnaires, which allowed an epidemiologic link to the laboratory-confirmed results. Because of the increased submission of questionnaires, AFIOH could compile a review of vaccine effectiveness and a virus-specific review of influenza-like illness

<sup>1</sup> ASD-HA Policy Memo No. 99-008, "Policy for DoD Global, Laboratory-Based Influenza Surveillance," 3 February 1999.

<sup>2</sup> US Department of Defense, Office of the Assistant Secretary of Defense for Homeland Defense (ASD-HD). Department of Defense Implementation Plan for Pandemic Influenza, task no. 4.2.3.8, August 2006.



## Identification of Novel Strains Contributes to Influenza Vaccine Composition Two Years in a Row



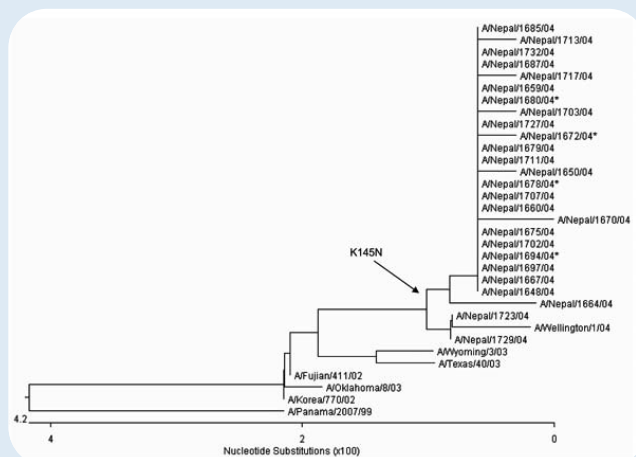
Accurate prediction of the strains to be included in the annual influenza vaccine depends on selection of the most prevalent circulating strains, the early recognition of threatening viruses, and accurate description of their ability to spread and to cause disease. In two consecutive years, selection of strains for the influenza vaccine was based on work by the broad GEIS surveillance network that began with refugees in southeastern Nepal and involved specimen collection by WARUN in Nepal, initial processing at AFRIMS in Thailand, and laboratory analysis at AFIOH in Texas.

AFRIMS-GEIS conducts ongoing surveillance among Bhutanese political refugees in three camps in southeastern Nepal. In 2004 and 2005, this surveillance detected an off-season outbreak of influenza. Clinical samples were collected by WARUN and sent to AFRIMS and then to AFIOH for identification as a potentially threatening variant influenza strain. Early surveillance data and persistent laboratory work over several months led to the appropriate decision for the vaccine formulation in 2005 and 2006.

### 2005–2006 Vaccine: Influenza A

Molecular analysis was performed by AFIOH on several isolates from the 2004 outbreak among the refugees in July. Four noteworthy amino acid changes were observed within most of the isolates, and these changes were located within or immediately adjacent to sites known to bind neutralizing antibodies, indicating that existing antibodies to influenza A (H3N2) would have no or reduced effect. The spread and genetic change of this H3N2 strain were monitored until it reached the United States in February 2005.

In cooperation with the CDC, several isolates were subjected to extensive antigenic analysis in which most were shown to be distinct from the 2004 A/Fujian-like vaccine strain.



Unrooted phylogenetic analysis of HA1 hemagglutinin nucleotide sequences from 26 influenza A Nepal isolates along with the H3N2 vaccine strain and reference strains. Nepal isolates drifted from 2004–2005 A/Fujian/411/03 vaccine strain (and A/Wyoming/03/03 vaccine seed strain) and are genetically equivalent to A/California/7/04, the 2005–2006 Northern Hemisphere vaccine strain. Arrow, K145N substitution was observed in 24 of 26 Nepal isolates and represents a genetic marker for the dominant lineage of H3N2 viruses during the 2004–2005 season.

\* Isolates that were antigenically distinct from A/Wyoming/303.

## Identification of Novel Strains – Continued

Influenza A (H3N2) viruses containing these key amino acid changes were officially recognized in the United States in February 2005. This novel influenza virus emerged during the 2005–2006 season as the dominant strain worldwide. As a result, WHO changed the A/Fujian strain for the 2005–2006 vaccine to A/California/7/2004, a virus that included all the mutations observed within the Nepalese strains.

### 2006–2007 Vaccine: Influenza B

During May and July 2005, AFIOH isolated influenza B virus from specimens from the Bhutanese refugees and from another outbreak at Luke Air Force Base (Arizona). Several isolates were genetically characterized by nucleotide sequencing of the viral genome and were shown to be members of the B/Victoria lineage, a family of influenza B viruses that were not represented in the Northern Hemisphere vaccine strain during the 2005–2006 season. Antigenic testing at the CDC in FY06 confirmed that these influenza B isolates were distinct from the vaccine strain and reference strains from B/Victoria lineage. Furthermore, genetic inspection of other influenza genes revealed that these novel viruses contained some genes from the B/Victoria lineage and other genes from the B/Yamagata lineage. Collectively, these genetic and antigenic findings indicated that these viruses differed from previously circulating influenza B viruses, and these differences prompted the WHO to change the influenza B component of the 2006–2007 vaccine.



Outbreak of influenza A occurred in three Bhutanese refugee camps in remote southeastern Nepal (green circle). Data gleaned from specimens collected from these refugees contributed to the vaccine strain selection in two consecutive years, demonstrating the value of the robust global surveillance supported by GEIS.



symptoms. Both reviews were presented at national meetings: the vaccine effectiveness data at the DoD Global Influenza Working Group meeting in San Antonio in May 2006, and the influenza-like illness data at the Syndromic Surveillance Conference in Baltimore in October 2006.

A total of 4,303 respiratory specimens were processed during the 2005–2006 season (2 October 2005–30 September 2006). For specimens having a completed result, 37 % were positive for a respiratory virus, and 29 % were positive for influenza. Influenza A was the predominant influenza type circulating throughout the season, accounting for 77 % of the influenza isolates identified. All AFIOH respiratory data, including 120 isolates and 101 original samples, were shared with the CDC and WHO to support decision making regarding seasonal trivalent influenza vaccine composition for the 2006–2007 season.

## Response

Routine interaction with sentinel sites increased awareness and participation this season as AFIOH submitted site-specific weekly notification to GEIS of 1) laboratory-confirmed results, 2) influenza-like illness activity, 3) sentinel site surveillance reports, and 4) overall surveillance reports. In the event of an emerging pathogen, pertinent email and voice mail messages were and will continue to be sent to those who need the information.

Laboratory results are coupled with demographic data and analyzed on a biweekly basis. Influenza-like illness is reviewed daily using DoD syndromic surveillance systems and weekly using the Standard Ambulatory Data Registry (SADR) as an indicator for specimen submission. When patient visits for a respiratory condition increase at a site, AFIOH contacts the site points of contact to assess adequate specimen collection. In the 2006–2007 season, AFIOH will expand SADR surveillance from the Air Force to the entire DoD and will analyze DoD-wide influenza-like illness cases in the Standard Inpatient Data Registry. An electronic summary describing surveillance and influenza-like illness activity is prepared weekly, and programmatic reports and presentations are produced routinely for public health personnel, including the CDC Epidemic Information Exchange and selected conferences worldwide. AFIOH also studied

influenza vaccine breakthroughs (i.e., cases in which influenza was contracted despite vaccination) in all active duty Air Force personnel. Molecular analysis of the influenza A hemagglutinin gene revealed that the viral strains infecting vaccinated personnel were related to but different from the strains used in the 2005–2006 vaccine.

A sentinel site in southeastern Nepal, maintained in collaboration with AFRIMS in Bangkok, experienced a third influenza outbreak in 3 years among Bhutanese refugees in July 2006. The full-length hemagglutinin coding region was sequenced from 21 isolates obtained during the outbreak. A nucleotide sequence comparison among the strains obtained from Nepal revealed a high level of sequence homology, as would be expected from geographically related isolates. Interestingly, 86 % (18/21) of the isolates contained four defining amino acid changes compared with previous H3N2 vaccine strains (A/California in 2005–2006 and A/Wisconsin in 2006–2007). All 21 Nepal isolates were genetically similar to the 2006–2007 A/Wisconsin/67/2005 vaccine strain.

## Capacity Building

AFIOH provided increased diagnostic and reporting capability at both AFRIMS (Bangkok) and NMRC (Lima). Training involved the use of the RAPIDS real-time thermocycler and the primers and probes for universal influenza A; universal influenza B, H1, H3, H7; and the new H5 assay. One objective of this training was to provide a means to identify the strain of influenza at the forward location to detect unique influenza subtypes earlier after patient presentation. AFIOH provided a standard reporting and analysis mechanism for AFRIMS. Routine surveillance reporting was streamlined in the SPSS statistical software package.

Ongoing training includes collective participation in national and international conferences, such as the Vaccines and Related Biological Products Advisory Committee, the International Conference for Emerging Infectious Diseases, the Asia-Pacific Military Medicine Conference, and the Council for State and Territorial Epidemiologists, along with routine publications in scientific journals. All published sequence data were given to the National Center for Biotechnology Information GenBank sequence database, an annotated collection of all publicly available DNA sequences.

## Naval Health Research Center

As the chief organization for surveillance of respiratory illness affecting military personnel in the Navy and at all initial entry military training centers, the Naval Health Research Center (NHRC) in San Diego is a critical partner in the GEIS network for infectious disease surveillance. NHRC was instrumental in demonstrating increased adenoviral morbidity among basic trainees after loss of the vaccine in the military in the late 1990s and remained involved in the restoration of the adenovirus vaccine program by supporting large, two-site, Phase III efficacy trials of adenovirus 4 and 7 vaccines at two basic training centers. During the past decade, NHRC has continually expanded its scope of studies and diagnostics, with an increased emphasis on influenza. Molecular capabilities, in particular, have been greatly enhanced, and NHRC has become a leading reference laboratory for respiratory disease work within the DoD. During FY06, NHRC doubled laboratory testing capacity for influenza, began construction of a BSL-3E laboratory, and conducted several projects sponsored by GEIS that contributed to force health protection.

### Surveillance

Through GEIS, NHRC conducted surveillance for febrile respiratory illness (FRI) among basic training, deployed shipboard, and Mexican border populations during FY06 (Figure 5). Basic training centers and ships have always carried a high risk of respiratory disease transmission, so GEIS is interested in the behavior of pathogens in both environments. Border surveillance is crucial because border populations could bring novel influenza strains or other respiratory pathogens into the United States at a point where military forces are heavily concentrated.

The number of FRI specimens collected and frequency of shipments from eight initial entry training centers was increased to provide more robust and timely influenza surveillance. An early season influenza A/H1N1 cluster was identified at Marine Corps Recruit Depot (MCRD) San Diego in August 2006. Calculation of influenza vaccine effectiveness among basic trainees throughout the DoD showed that the 2005–2006 vaccine was 92 % effective in preventing laboratory-confirmed influenza (Figure 6). For the basic trainees, all of

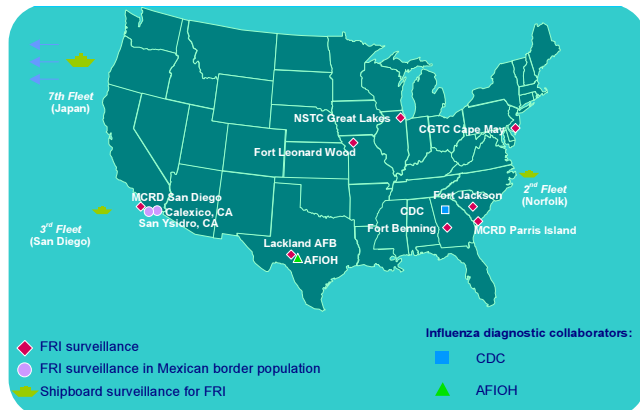


Figure 5. Sites within United States for DoD surveillance for febrile respiratory illness conducted by NHRC.

whom are vaccinated, there were 71 influenza A cases, eight of whom had been vaccinated at least 14 days before illness, and 21 cases of influenza B, six of whom had been vaccinated at least 14 days before illness.

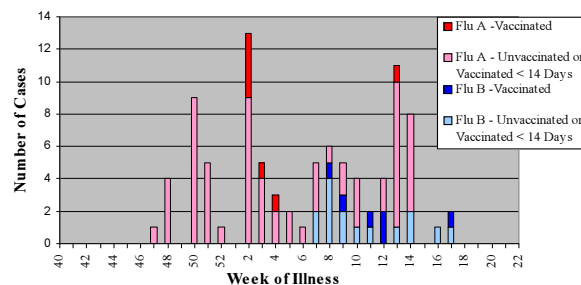


Figure 6. Vaccination status of confirmed influenza cases among basic trainees in 2005–2006, showing effectiveness of influenza vaccine.

Genome typing of adenovirus isolates established that seven different subtypes of type 4 adenovirus exist at the eight basic training centers and that each training center tends to have a specific subtype. This information was critical to ongoing efforts to restore the adenovirus vaccine among basic trainees, an effort that progressed this year to Phase III vaccination trials. NHRC surveillance of pneumonia cases throughout the DoD is ongoing, and preliminary results indicate that adenovirus, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* are the pathogens most frequently associated with pneumonia.



Shipboard FRI surveillance in the 3rd Fleet (eastern Pacific) identified clusters of influenza cases among sailors aboard several ships after port stops throughout the world, including areas thought to be at increased risk for pandemic influenza strains. Isolates from these cases were grown at NHRC and provided valuable strain and sequence information to the global surveillance community while providing operational support for forward-deployed servicemembers. During FY06, NHRC expanded shipboard FRI surveillance to the 2nd Fleet (Atlantic) and 7th Fleet (western Pacific), providing surveillance among these deployed populations for the first time.

Mexican border FRI surveillance was conducted at two sites during FY06; 223 FRI cases were enrolled through the end of the influenza season, with influenza A identified in over 40 % of the cases. Border surveillance provided some of the earliest influenza A isolates of the 2005–2006 season and provided valuable information regarding the current circulating influenza strain and the performance of a widely used rapid diagnostic test (Figure 7). Border surveillance involved effective interagency cooperation with the CDC and AFIOH, all of which support the GEIS pillar of integration and the DoD influenza surveillance system.

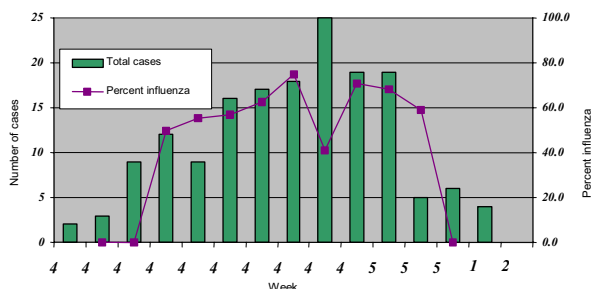


Figure 7. Data from NHRC-GEIS surveillance along Mexican border that provided isolates of influenza A early in 2005–2006 season, showing incidence of influenza-like illness and percentage of patients diagnosed with influenza A.

In FY06, NHRC performed genetic sequencing of influenza isolates obtained from all surveillance populations. Findings and isolates were shared with local, state, DoD, and CDC influenza surveillance partners. Isolates from the 2005–2006 season were most closely related to the A/Wisconsin strain, which was chosen as the H3 strain for the 2006–2007 vaccine. This GEIS work at NHRC illustrates the essential interagency cooperation that GEIS fosters. One direct result was the

2006–2007 vaccine, which was based on results obtained by NHRC from testing at MCRD San Diego the previous year.

## Response

The GEIS surveillance system at NHRC identified an early season cluster of influenza A at MCRD San Diego in August 2006. Laboratory staff quickly determined that an H1N1 strain was responsible and that none of the individuals had been vaccinated. Information was immediately shared with MCRD San Diego, GEIS, CDC, and local public health officials. FRI surveillance was intensified at this site for several weeks until it was determined that transmission had ceased. Training operations at the base were allowed to continue uninterrupted, in large part due to the epidemiologic data provided by NHRC.

Four separate outbreaks of group A streptococcal illness among basic trainees occurred during FY06, and NHRC provided laboratory and epidemiologic support for all. Emm type 5 *Streptococcus pyogenes* was the predominant subtype isolated in all four outbreaks. An outbreak of severe pneumonia that required hospitalization of some patients occurred among Navy SEAL trainees in March 2006. NHRC was notified and worked with NEPMU5 to obtain and test specimens from the outbreak. Testing identified *S. pneumoniae* (type 31) as the etiologic agent, and appropriate treatment and prophylaxis were initiated.

NHRC also provided laboratory support for 11 fatal or severe respiratory illness cases during FY06. Most of these were referred through the GEIS mortality surveillance program at the Armed Forces Institute of Pathology. Key findings included determination that emm type 5 *S. pyogenes* was isolated in two fatal cases among active duty servicemembers in Texas and that *S. pneumoniae* was associated with another fatal case.

Weekly updates that included influenza and FRI rate data were provided by NHRC to GEIS and other surveillance partners throughout the year. NHRC provided rapid laboratory confirmation of adenoviral etiology during FRI rate spikes that were identified by the FRI surveillance program. These spikes occurred at six of eight basic training camps under surveillance during FY06.

## Innovation

NHRC has incorporated triangulation identification for genetic evaluation of risks (TIGER) testing into its surveillance activities. TIGER is a high-throughput diagnostic platform that uses polymerase chain reaction (PCR) in conjunction with mass spectrometry to rapidly identify viral and bacterial pathogens with high sensitivity and specificity. This cutting edge technology has been validated for influenza and was used to rapidly determine that type A/H1N1 influenza was responsible for the MCRD San Diego FRI cases. The TIGER system implemented at NHRC through GEIS is one of only four such instruments in operation in the world.

During FY06, NHRC used its archive of original patient specimens to investigate the performance of new influenza diagnostics. One diagnostic technique, LoopAmp, showed promise as an accurate and easily used field diagnostic that would be ideal for shipboard and deployed settings where space and technical expertise are limited. NHRC is also working with Arbor Vita Corporation (Sunnyvale, CA) to validate a simple antibody-antigen strip test for H5N1 influenza.

Influenza vaccine effectiveness estimates are generally available only after the influenza season has concluded. Throughout FY06, NHRC investigated novel surveillance strategies that will utilize web-based information aggregation systems to forecast influenza vaccine effectiveness and avian influenza movement into the United States in the 2006–2007 season.

## Capacity Building

NHRC planned and began construction of a BSL-3E (enhanced) laboratory during FY06. This

laboratory will be operational in mid FY07 and will allow NHRC to grow highly pathogenic influenza strains and other dangerous microbes, providing DoD with unique capabilities. When completed, this facility will be one of eight BSL-3E laboratories in DoD in FY07 that could handle H5N1 avian influenza isolates in a pandemic.

Expansion of shipboard FRI surveillance into the 2nd Fleet and 7th Fleet is enhancing DoD capacity to identify and preserve isolates from influenza cases occurring among servicemembers deployed to high-risk areas throughout the world. NHRC established a Pacific Rim surveillance hub during FY06 to facilitate expansion of FRI surveillance into the 7th Fleet. The US Naval Hospital in Yokosuka, Japan, provided office and laboratory space for the Pacific Rim surveillance hub, and an on-site surveillance coordinator was hired in August 2006. In addition to engaging ships within the 7th Fleet, the coordinator is working with AFIOH to ensure that their sentinel influenza sites within the region are participating to the greatest extent possible.

NHRC provided on-site training and reagents to NEPMU5, NEPMU6, and Naval Hospital Okinawa to perform rapid PCR testing for adenovirus, influenza A/B, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*, utilizing their existing PCR equipment. Diagnostic capability for H5N1 avian influenza was provided in coordination with the CDC Laboratory Response Network. Naval Hospital Yokosuka is scheduled to receive this training in early FY07. NHRC also provided training, culture media, and rapid point-of-care influenza tests to two clinics that participated in the border FRI surveillance project.

## United States Army Medical Research Institute of Infectious Diseases

### Pandemic Influenza Surveillance

GEIS work at the US Army Medical Research Institute of Infectious Diseases (USAMRIID) in pandemic influenza surveillance in FY06 comprised an analysis of influenza molecular diagnostics, generation of an influenza A reference panel, and

development of immunodiagnostic reagents for influenza diagnosis. Various real-time PCR avian influenza assays were identified, acquired, and evaluated. A comparison of the assay developed by Idaho Technology (Salt Lake City, UT), the advanced developer for the DoD Joint Biological Agent Identification and Detection System, was



included. All evaluations were conducted with H5N1 avian influenza RNA collected in the field by NAMRU-3 (Cairo, Egypt).

The USAMRIID first analysis of six published or commercial molecular diagnostic assays for highly pathogenic avian influenza has demonstrated that the CDC Laboratory Response Network H5N1 assay was the most robust of the assays tested. This finding supports the deployment of the assay within the Military Health System (MHS) for identification of personnel potentially infected with the H5N1 strain of highly pathogenic avian influenza.

GEIS supplemental funding for pandemic and avian influenza was the only source of funding for USAMRIID work with highly pathogenic avian influenza in FY06. Further analytic studies are limited until the expansion of the influenza reference panel is completed. Sources for viruses were identified for both the highly pathogenic and low pathogenic strains of influenza. Specialized equipment for highly pathogenic avian influenza work was purchased, and personnel were trained in biosafety practices specific for this pathogen. USAMRIID provides DoD and GEIS with a unique high containment laboratory capable of supporting work with highly pathogenic avian influenza.

### **Detection and Identification of Infectious Diseases Requiring High Level Biological Containment**

In FY06, USAMRIID continued to serve as a national resource for the isolation and identification of highly pathogenic infectious disease agents in addition to influenza that require handling at biosafety levels 3 and 4. USAMRIID has the only biosafety level 4 (BSL-4) containment medical suite in DoD where patients infected with highly contagious unknown or nontreatable infections can be diagnosed and treated safely. In this capacity,

USAMRIID served as a DoD and WHO reference center for hemorrhagic fever and other arthropod-borne viruses. This is accomplished through testing of clinical samples and the close interaction with submitting clinicians and diagnosticians to identify the disease-causing pathogen and determine the appropriate course of treatment.

USAMRIID also provided confirmatory diagnostic support for many overseas and domestic laboratories including those within the GEIS network. Development and fielding of new diagnostic assays, technology transfer to other government and civilian organizations, production and stockpiling of critical reagents, and an ability to respond rapidly to outbreaks of emerging and reemerging diseases have been important components of the USAMRIID program. GEIS support enabled USAMRIID to maintain its capabilities in diagnostics of infectious diseases through the development and testing of assays. Collaborations with the DoD overseas laboratories offer unique opportunities to field test assays while providing valuable reagents and expertise to GEIS collaborators.

The USAMRIID effort directly supports the GEIS pillars of response and readiness and is essential for the protection of the warfighter. GEIS diagnostic readiness is maintained through the constant renewal of diagnostic reagents for testing and development of improved and new assays. Diagnostic training of military and civilian personnel and organizations is manifested through USAMRIID support of the field identification of biological warfare agents course. This is accomplished by supplying diagnostic reagents, specific agent assays, and additional training and consultation for students and instructors, as needed. Through the GEIS program, USAMRIID maintains the ability to respond to disease outbreaks in the field and/or support collaborators responding to arthropod-borne and hemorrhagic fever virus outbreaks on a global scale.

## **Naval Medical Research Center**

Through GEIS, four new quantitative real-time PCR assays were developed by the Naval Medical Research Center (NMRC). These assays were used by the DoD overseas laboratories to determine the risk of rickettsial diseases in military beneficiaries

and foreign host country populations. NMRC also trained personnel at the overseas laboratories to perform the assays and acts as a reference laboratory for confirmatory tests.

Rickettsial and related diseases, including epidemic typhus, murine typhus, Rocky Mountain spotted fever, Mediterranean spotted fever, scrub typhus, ehrlichiosis, and trench fever, are endemic or reemerging in much of the developing world. Antibiotic resistance and prophylaxis breakthroughs have been reported with *Orientia tsutsugamushi*, the agent of scrub typhus. A need continues for a DoD reference laboratory to confirm serologic and molecular biologic detection results and to culture live rickettsiae in BSL-3 laboratories.

Rickettsial diseases are serious vector-borne infections to which servicemembers may be exposed, so DNA-based and serological identification of infected or exposed military personnel is an asset to the MHS supported by GEIS. Rickettsial diseases are difficult to diagnose because symptoms are often nonspecific and share characteristics with other febrile illnesses. Rapid serologic tests, such as the nonspecific Weil-Felix test and the *Rickettsia*-specific enzyme immunoassays and rapid flow devices, provide some epidemiologic data, but sensitivity is limited by the delay in onset of host

antibodies, which is usually 7–21 days after onset of disease. Furthermore, specificity is limited by the variations and cross-reactivity in antigens among rickettsial groups, species, and even serotypes within a species. Complex indirect immunofluorescence assays can increase accuracy. The preparation of reagents for the gold standard serodiagnostic assays such as ELISA, indirect immunoperoxidase assay, and the immunofluorescence assay require the propagation of rickettsiae in infected yolk sacs of embryonated chicken eggs or cell cultures. To detect emerging species and strains as causes of human disease, isolation of the causative agent is necessary. However, isolation is hazardous and requires special training and a BSL-3 laboratory because of the high risk of laboratory-acquired infections.

The NMRC is ideal for performing, training others to perform, and developing rickettsial diagnostic assays because personnel routinely conduct serological assays, molecular biology assays, and isolation techniques (Table 1). In addition, BSL-3 laboratories at NMRC are dedicated to work with rickettsiae.

**Table 1. Reagents and Assays Produced by NMRC**

Disease	Agent	Serology	Assay
<b>Scrub typhus group</b>			
Scrub typhus	<i>O. tsutsugamushi</i>	IFA, ELISA, WB	PCR, quantitative real-time PCR
<b>Rickettsioses</b>	<i>Rickettsia</i> genus-specific		PCR, quantitative real-time PCR
<b>Typhus group</b>			
Epidemic typhus	<i>R. prowazekii</i>	IFA, ELISA, WB	PCR, quantitative real-time PCR
Murine typhus	<i>R. typhi</i>	IFA, ELISA, WB	PCR, quantitative real-time PCR
<b>Spotted fever group</b>			
Tick-borne rickettsioses	Group specific	IFA, ELISA, WB	PCR, quantitative real-time PCR
Rocky Mountain spotted fever	<i>R. rickettsii</i>	IFA, ELISA, WB	PCR, quantitative real-time PCR
Boutonneuse fever	<i>R. conorii</i>	IFA, ELISA, WB	PCR, MLST
African tick bite fever	<i>R. africae</i>	IFA, ELISA, WB	PCR, MLST
Flea-borne spotted fever	<i>R. felis</i>	ELISA	PCR, quantitative real-time PCR
Unknown	<i>R. montanensis</i>	ELISA	PCR, quantitative real-time
Unknown	<i>R. amblyommii</i>	ELISA	PCR, quantitative real-time PCR
Tidewater spotted fever	<i>R. parkeri</i>	ELISA	PCR, MLST
<b>Ehrlichiosis and anaplasmosis</b>			
Human monocytic ehrlichiosis	<i>E. chaffeensis</i>	IFA	PCR, quantitative real-time PCR
Human granulocytic anaplasmosis	<i>A. phagocytophila</i>	ELISA, WB	PCR, MLST
<b>Bartonella group</b>			
Bartonellosis	<i>B. bacilliformis</i>	under development	PCR, quantitative real-time PCR
Trench fever	<i>B. quintana</i>	IFA	PCR, quantitative real-time PCR
<b>Borrelia</b>			
Relapsing fever	<i>B. recurrentis</i>		PCR, quantitative real-time PCR
Lyme disease	<i>B. burgdorferi</i>	commercial assays	
Southern tick-associated rash illness	<i>B. lonestari</i>		PCR, quantitative real-time PCR

NMRC has developed three FDA-cleared tests for typhus, spotted fever, and scrub typhus: ELISA, Dip-S-Ticks, and rapid flow devices. GEIS supports NMRC reference laboratory functions and rickettsial diseases research at all five DoD overseas laboratories. NMRC has acted as the reference laboratory for these sites and others and provides reagents, technical expertise, and training.

After the development of two new quantitative real-time PCR assays for *R. typhi* (murine typhus) and *R. felis* (flea-borne spotted fever) this year, NMRC used the assays to determine the presence of rickettsiae in *Xenopsylla cheopis* (Oriental rat flea), the known vector of plague and murine typhus collected in Malang, Indonesia, by NAMRU-2. The study showed that not only *R. typhi* but also *R. felis* was identified in the fleas, and the report was the first to describe the presence of the human pathogen *R. felis* in Indonesia. The report also showed for the first time that *R. felis* can be found in *X. cheopis*, suggesting that the Oriental rat flea may also serve as an important vector of flea-borne spotted fever, similar to *Ctenocephalides felis* (cat flea).

In laboratory-based surveillance conducted by NAMRU-3 for acute febrile illness in Egypt, ~6% of patients were found to be positive for typhus group rickettsioses, as documented by a four-fold rise in titer by the NMRC typhus group ELISA. These results indicate the quality of the NMRC test, and the strength of the NAMRU-3 surveillance program is demonstrated by the acquisition of serial blood

specimens. In addition, one patient was determined to be positive by real-time PCR assay for *R. felis*.

NMRC developed two new assays to detect *R. montanensis* and *R. amblyomma* that were used to determine the presence of these frequently found rickettsiae in ticks found feeding on DoD personnel and their dependents throughout the United States. The prevalence in ticks of *R. montanensis* was 2.1% (17/808) and *R. amblyommii* was 66.3% (246/371).

The NMRC real-time PCR assays and multilocus sequence typing techniques were used to determine that a servicemember with spotted fever rickettsiosis was infected with *R. parkeri*. This is only the second reported case of *R. parkeri* associated with human disease even though the agent has been known for more than 65 years as a common tick-associated *Rickettsia*.

Through GEIS, data are currently being collected to determine the risk of rickettsial disease to military personnel stationed in or deployed to South Korea in support of 18th MEDCOM. Sera from ~1,000 of 10,000 samples from military personnel previously stationed in South Korea were obtained from the DoD Serum Repository and have been assessed for antibodies specific for spotted fever, typhus, and scrub typhus rickettsiae. Additional GEIS-supported investigations utilizing NMRC reagents and assays are in progress throughout the world.

## Walter Reed Army Institute of Research

### Malaria Diagnostics Training Center in Kisumu, Kenya

The quality of laboratory medicine is often a barrier to effective health care, public health surveillance, and research in the developing world. Reliable laboratory endpoints are required for clinical trials, monitoring the occurrence of illness, and outbreak investigations. To improve laboratory capacity, GEIS has actively been pursuing quality laboratory testing with a particular focus on a challenging diagnostic test, malaria microscopy.

Malaria microscopy, considered by many the gold standard for diagnosis, has documented limitations. Efficacy estimates in drug and vaccine malaria prevention trials are sensitive to small errors in microscopy endpoints, so accurate and reproducible results are required. GEIS partnered with the Walter Reed Army Institute of Research (WRAIR) to establish a malaria diagnostics center of excellence in Kisumu, Kenya, in 2004 to ensure valid clinical trial and diagnostic test evaluations and to improve diagnostic capacity in Kenya and elsewhere. With GEIS support, the WRAIR Experimental Therapeutics Division developed

a 2-week (long) and a 1-week (short) training course for microscopists working in the developing world in clinical and public health settings. The courses consisted of supervised laboratory practical examinations, lectures, group discussions, demonstrations, and take-home assignments. Well-characterized slides and training materials were iteratively improved. Objective pre- and postcourse evaluations consisted of 30 slides (19 negative, 11 positive) with a density range of 50–660 parasites/μl, a written examination (65 questions), a photographic image examination (30 images of artifacts and species specific characteristics), and a grid counting examination.

Through FY06, 209 microscopists from 11 countries have been trained in malaria diagnostics: Kenya ( $n = 178$ ), Uganda ( $n = 10$ ), Tanzania ( $n = 5$ ), Rwanda ( $n = 1$ ), Burundi ( $n = 1$ ), Malawi ( $n = 6$ ), Cameroon ( $n = 3$ ), Mali ( $n = 2$ ), Nigeria ( $n = 2$ ), and Thailand ( $n = 1$ ). The following results were achieved:

- Sensitivity improved by a mean of 14 % (CI 9–19 %) from 77 % (CI 73–81 %) baseline;
- Specificity improved by a mean of 17 % (CI 11–23 %) from 76 % (CI 70–82 %) baseline;
- A refresher course for people who had previously completed this training showed continued improvement with a mean final sensitivity of 95 % (CI 91–98 %) and specificity of 97 % (CI 95–100 %);
- Operational research showed that a grid method for counting does not improve accuracy, that thin smear examination is more sensitive than anticipated, and that cross-contamination is a problem during batch staining.

False-positive and false-negative malaria smears are a serious problem, even for research microscopists, and rigorous systematic training dramatically improved performance. This project has shown that quality microscopy can be achieved using intensive training and examination at a center of excellence. This model may be useful for other diagnostic problems of public health importance and disease control strategies.

## Malaria Drug Resistance Surveillance

The methodology and approach to describe antimalarial drug resistance demand adherence to rigorous clinical and parasitological criteria. The

GEIS OCONUS infrastructure grounded in the five DoD overseas laboratories provides unique opportunities to elucidate the mechanisms of drug resistance and to better predict the public health implications of emerging drug resistance in the field.

The WRAIR Division of Experimental Therapeutics has developed tools to document drug resistance in the parasites that cause malaria. These include known clinical outcomes, pharmacokinetics, molecular markers, and culture capabilities. The division is pursuing harmonization of protocols and focusing on a program that collects data from the protocol studies in real time in a shared database to discern patterns of resistance. These patterns can facilitate practical decisions on DoD drug policy in different geographic regions and further knowledge of the pressures that drive selection to drug resistance.

## Antimalarial Studies

GEIS supported four antimalarial WRAIR studies in Africa, three on civilian patients and one in the military setting. Results provided data to help determine the best defense against malaria for the military, host nations, and travelers in these regions. In addition, GEIS supported WRAIR participation in two meetings addressing global antimalarial resistance. This work particularly supports the GEIS pillar of readiness.

**Amodiaquine.** To document amodiaquine resistance, the association among *Plasmodium falciparum* chloroquine resistance transporter (pfcrt) T76, *P. falciparum* multidrug resistance gene 1 (pfmdr1) Y86 alleles, and in vivo amodiaquine resistance was studied. The clearance of parasites harboring these two alleles in children treated with amodiaquine in southwest Nigeria was studied: 101 children with acute uncomplicated *P. falciparum* malaria infections were treated with the standard dosage of amodiaquine and followed for 28 days. Blood samples were collected at enrollment and during follow-up for identification of parasite genotypes and pfcrt and pfmdr1 mutations using PCR and restriction fragment length polymorphism approaches. The identification of the combination of mutant pfcrtT76 and pfmdr1Y86 alleles may be useful markers for monitoring the development and spread of amodiaquine resistance when combining this drug with other antimalarials for treatment in Africa.



**Atovaquone.** In vitro and in vivo resistance of *P. falciparum* to atovaquone or atovaquone-proguanil hydrochloride combination has been associated with two mutations in the parasite's cytochrome *b* gene. However, little is known about the prevalence of specific mutations in cytochrome *b* within natural populations of *P. falciparum* that have had no previous exposure to the drug in Africa. Consequently, the prevalence of specific mutations in the cytochrome *b* gene of African *P. falciparum* isolates from Nigeria, Malawi, and Senegal, where atovaquone-proguanil has not been introduced for treatment of malaria, was assessed: 295 samples from the three countries were analyzed for mutations previously associated with antimalarial resistance. Most of the isolates tested did not encode any mutations in cytochrome *b* that have been shown to be associated with drug resistance. However, 4 % of the isolates from Nigeria were found to harbor mutations known to confer atovaquone resistance even though the drug had not been used to treat malaria patients. This is the first reported evidence of cytochrome *b* mutation in unexposed *P. falciparum* isolates from Nigeria. The emergence in Africa of *P. falciparum* isolates with cytochrome *b* mutation is a matter of serious concern related to malarial treatment. Based on this study, GEIS recommended continuous monitoring of atovaquone-proguanil-resistant *P. falciparum* in Africa for the rational use of this new antimalarial, especially in nonimmune travelers.

**Chloroquine.** Chloroquine resistance in *P. falciparum* is associated with polymorphisms in two specific genes of the parasite. This study examined the association between parasites that encoded these two mutant genes and chloroquine resistance. The association between in vivo chloroquine resistance and *P. falciparum* genetic mutations in these two genes was determined in isolates obtained from 111 children with acute uncomplicated *P. falciparum* malaria in Nigeria. Patients were treated with a standard dosage of chloroquine and followed for 28 days. Of the 111, fifty-five failed treatment. Mutant alleles found in 84 % were associated with in vivo chloroquine resistance. In addition, the mutant alleles were significantly selected for by chloroquine in patients who failed treatment. Considering the high level of chloroquine resistance and drug use in the study area, these results indicate that use of this antimalarial will continue selection for resistant parasites.

**Mefloquine.** During 2006, only one *P. falciparum* malaria specimen was received from an active duty patient who had traveled to Nigeria and acquired malaria. This specimen was resistant to chloroquine, pyrimethamine, and quinine and exhibited a modest decrease in susceptibility to mefloquine, which has been observed in West Africa. Mefloquine is a standard malaria prophylactic regimen for travelers to West Africa, but data on mefloquine resistance are scarce in many parts of the region. Because of concern for reduced mefloquine sensitivity in West Africa, a retrospective analysis of *P. falciparum* infection among US Marines deployed to Monrovia, Liberia, in 2003 was conducted in which mefloquine resistance patterns in archived isolates and data from previous studies were compared. Data on *P. falciparum* isolates from the Marines obtained after the 2003 deployment to Monrovia were used, along with other archived *P. falciparum* isolates and a systematic literature review, to assess mefloquine resistance in Liberia. During the 2-week deployment, 80 of 225 Marines contracted *P. falciparum* malaria (the official investigation implicated missed doses of mefloquine in the high attack rate). Pretreatment isolates were obtained for eight patients, and sensitivity to 17 drugs was assessed using radioisotopic methods. These results suggested that there may be reduced sensitivity to mefloquine in Liberia. Considering the paucity of current data, in vitro and in vivo studies are needed to further assess mefloquine resistance in Liberia and the rest of West Africa.

### Professional Meetings

GEIS supported WRAIR participation in two meetings addressing the global problem of antimalarial resistance. At the Fourth Multilateral Initiative for Malaria Pan-African Malaria Conference in Yaounde, Cameroon, in November 2005, a keynote address was given by a WRAIR staff member on alternatives for worldwide collaboration to collect information on the response of patients to drug treatment and the response of parasites to drugs in vitro.

A follow-up symposium was presented at the American Society of Tropical Medicine Meeting in Washington, DC, and was entitled "A Global Database of Antimalarial Drug Effectiveness: It's About Time." Symposium organizers described the yearlong GEIS participation in a coalition effort led

by the University of Washington to coordinate efforts to create a dynamic open-access database that would include current and historical data on clinical efficacy, pharmacokinetics, in vitro responses, and molecular markers related to drug resistance in *P. falciparum* and *P. vivax*. The coalition received support from the Gates Foundation for a follow-up meeting in October 2006 in the United Kingdom.

## Global Mapping and Modeling of Mosquito Vectors

### *Modeling for Potential Distribution of Mosquitos*

To address the increasing need for continental and global scale databases of mosquito populations, GEIS partnered with the WRAIR Division of Entomology (Walter Reed Biosystematics Unit; a joint program of WRAIR and the Smithsonian Institution) and 18th MEDCOM in South Korea to create a novel system to model the potential distribution of mosquitos in South Korea, Southeast Asia, and South America. This work supports the GEIS pillars of innovation, surveillance, and cooperation.

Ecologic niche modeling is a new tool that can be used to identify areas potentially at risk for infectious disease outbreaks in militarily important regions. This tool can help direct the resources required for mosquito control and disease prevention by forecasting disease transmission risk. Genetic algorithms and point occurrence data have been used to develop models for the major vector species of mosquito-borne human diseases (e.g., malaria and arboviral diseases). High-resolution maps of predicted disease vector locations could offer critical situational awareness about where these diseases can and cannot occur based on the presence and absence of the vector. In addition, these maps could be used as base layers in geographical information system models that use remotely sensed data to calculate the risk of disease transmission at any point in the world. Global mosquito maps could assist in decisions about locations of hospitals and bases, the type and extent of vector control and prophylaxis needed for an area, and quarantine and invasive species management.

For the projects described below, vector occurrence data were obtained for specimens housed in collections of the Smithsonian Institution and other museums and laboratories. The identities of these

specimens were confirmed by morphological or molecular techniques. Ecologic distribution parameters (e.g., diurnal range and precipitation) with the greatest effects on the models were determined.

### *Modeling Mosquito Vectors in South Korea and Southeast Asia*

Ecological niche modeling of geographic and occurrence records revealed the potential distribution of mosquito malaria vectors in South Korea and Southeast Asia. The Walter Reed Biosystematics Unit communicated this information to PACOM to heighten its awareness of infectious disease threats in the region.

PCR-identified specimen records of occurrence (1998–2004) were obtained for five mosquito malaria vector species of *Anopheles* (*Anopheles*) in South Korea (i.e., *A. sinensis* Weidman, *A. kleini* Rueda, *A. belenrae* Rueda, *A. lesteri* Baisas and Hu, and *A. pullus* Yamada). Geographic data or actual occurrence points were obtained from the literature for four mosquito malaria vector species of *Anopheles* (*Cellia*) of Southeast Asia: *A. dirus* Peyton & Harrison, *A. baimaii* Sallum and Peyton, *A. minimus* Theobald A, and *A. minimus* Theobald C. By using artificial intelligence (Desktop Genetic Algorithm for Rule Set Prediction) with Worldclim global climate layers ([www.worldclim.org](http://www.worldclim.org)) and environmental layers such as temperature, precipitation, bioclimatic, and hydrologic, preliminary ecologic niche models were prepared to predict the potential distributions of the mosquito malaria vectors in South Korea and Southeast Asia. Additional results of mosquito collections for *Anopheles* (*Anopheles*) species from South Korea in May 2006 were recently identified using PCR, and they will soon be analyzed and fit into the prediction models of vector distributions in the Korean peninsula and other parts of Asia. Preliminary results from Korea suggest that malaria risk may be concentrated near the Demilitarized Zone because likely vectors are restricted to the area.

### *Spatial Database of Mosquito Occurrence Records in South America*

The Walter Reed Biosystematics Unit examined the Smithsonian database of ~43,000 georeferenced records of 492 identified and vouchered



mosquito species from 42 countries throughout the neotropical region of South America that had been collected from 1,853 locations between 1899 and 1982. The examination revealed the location of hot spots in species richness and endemism and suggested areas where mosquito collection inventory needs are greatest for distribution prediction modeling.

The mosquito *Anopheles (Nyssorhynchus) albimanus* Wiedemann was the most common species recorded from several countries in the region. By using the ecologic niche model based on climate matching, the species of genus *Anopheles* had the largest predicted ranges, whereas species of genera *Deinocerites* and *Wyeomyia* had the smallest. Mosquito species richness was estimated for one-degree grids and by summing the predicted presence of species from the model. The collection records that were analyzed have been lodged with the Smithsonian online database, which could be used as a first step toward a global-scale repository of georeferenced collections of mosquitoes, including vectors of infectious human diseases.

### *Global Mosquito Biogeography from Country Species Records*

With data stored at the Walter Reed Biosystematics Unit (an effort jointly supported by WRAIR and the Smithsonian Institution; [www.mosquitocatalog.org/main.asp](http://www.mosquitocatalog.org/main.asp)), country occurrence records were analyzed for mosquito species of Culicidae, the family that includes all mosquitoes (Figure 8). The results indicated that mosquito occurrence shows a linear log-log species-area relationship and that island nations are more species-rich and have higher endemism than mainland nations.

A website at [www.mosquitomap.org](http://www.mosquitomap.org) will be developed to post global mosquito occurrence data and mosquito distribution models. Web-based presentations of potential distribution of mosquito vectors and related species will be developed. These tools and information sets will provide base-level estimates of disease risk for disease prevention strategies.

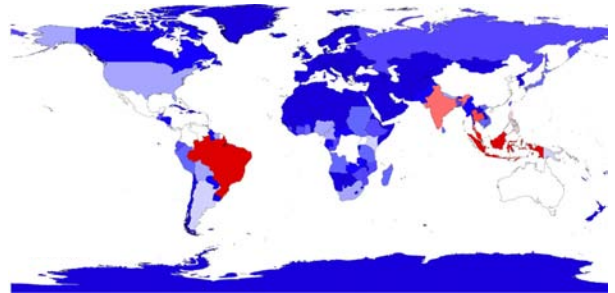


Figure 8. Map of total mosquito species per country generated by modeling of vector data available from specimens in Smithsonian systematic catalog of Culicidae. *Dark blue*, 0–89 species; *light blue*, 90–208 species; *white*, 209–268 species; *red*, 269–447 species.

### *Military Installation Pandemic Preparation*

The WRAIR Division of Preventive Medicine addressed the need for military public health response to an influenza pandemic by improving the capacity of installation-level preventive medicine services to effectively detect and respond to an outbreak. The work included the following:

- Analysis of current surveillance and response capabilities;
- Development of a mission essential task list;
- Development of detailed written guidance;
- Development of a web-based reportable medical events system;
- Development of training in epidemiology and disease surveillance.

Local public health responses to large or complex infectious disease outbreaks frequently rely on the involvement of external preventive medicine teams, such as those from CHPPM. These regional and strategic level teams deploy to provide expertise and personnel to local preventive medicine professionals. However, pandemic influenza will be a widespread public health emergency that will quickly overwhelm strategic support capabilities. This situation will require local preventive medicine organizations to operate independently for extended periods.

Local organizations must be equipped and prepared to perform surveillance, incident command, outbreak investigation, infection control, social distancing (quarantine and isolation), environmental health, occupational health, population-level

interventions (mass vaccine/ antiviral programs), liaison with civilian public health providers, and risk communication/ health information operations. The absence of an effective vaccine or antiviral early in the outbreak will make basic public health measures, such as social distancing, essential. A rapid and effective local response might be critical if a redeploying unit is the mechanism that introduces the virus into the United States, as has been suggested by the Armed Forces Epidemiology Board.

Many local public health organizations currently lack the infrastructure, plans, training, and equipment to manage a complex outbreak with limited external assistance. The first part of the Division of Preventive Medicine project was designed to better understand and then to enhance public health situational awareness and information flow during a pandemic. The key components included analyzing the doctrine, organizations, training, leader development, materiel, personnel, and facilities; hiring a computer programmer to assist in the development of a new web-based version of the Reportable Medical Events System; and developing tools, doctrine, and training to support key epidemiological and public health

leadership tasks at the installation level. The second part of the project was designed to correct deficiencies in local pandemic influenza surveillance and response capabilities. The main focus of the project was to provide equipment sets to local preventive medicine services to enhance public health incident command, communications, and epidemiological data collection, analysis, and reporting (Figure 9).

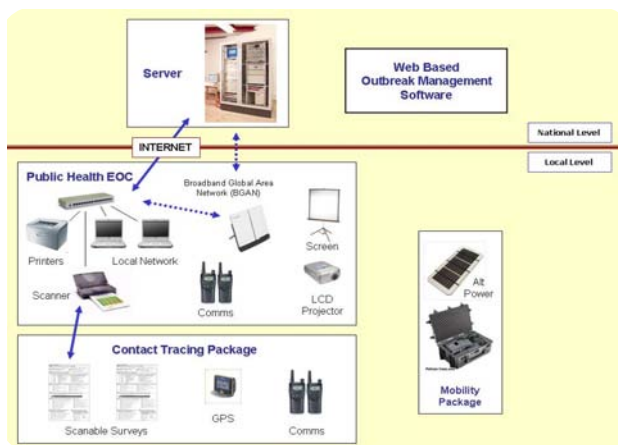


Figure 9. Working concept for equipment sets to be used at local level and supporting hardware and software to be used at national level during influenza pandemic.

## Armed Forces Institute of Pathology

### Directory of Public Health Laboratory Services

GEIS and the Armed Forces Institute of Pathology (AFIP) have created and maintain a password-protected searchable database containing information about nonroutine tests for infectious disease agents that supports MHS practitioners and clinical laboratory personnel. Until the establishment in 2000 of the Directory of DoD Public Health Laboratory Services through GEIS funding, no consolidated, up-to-date listing of specialized tests was available to the military services.

The need for the directory was articulated in September 1999 when a joint service Public Health Laboratory Workshop Group identified the absence of a DoD directory of laboratory tests, such as those needed during an outbreak or in support of troops

being rapidly deployed to areas of high risk for emerging infectious agents, as a weakness in the MHS. The 1999 workshop group concluded that the absence of such a directory and a supporting laboratory system to provide the services negatively affected military readiness.

The 1999 workshop group recommended that the AFIP implement and maintain a DoD directory of special tests, termed a Directory of Public Health Laboratory Services. It also recommended that steps be taken to tie DoD and civilian laboratories into a Virtual Public Health Laboratory network to support DoD beneficiaries globally. Since then the prototype Directory of DoD Public Health Laboratory Services, developed by the GEIS Headquarters, was reviewed at AFIP, updated, and implemented utilizing current industry-standard software and advanced search capabilities.

The directory is available at <https://afip-geis.afip.osd.mil> and is linked to the AFIP and GEIS websites. Access requires a password, and four levels of security are incorporated. Detailed data for biological agents and corresponding diseases are contained, and contact information for CONUS and OCONUS military laboratories that have the capabilities to test for these agents is listed. Laboratory directors can update their listings regularly. Illustrative clinical photographs and histologic images are provided along with direct links to additional information from the CDC, NIH, and WHO. Daily user activity is tracked to identify inquiries, which provides GEIS with another source of information that might alert surveillance efforts to new infectious disease activity.

The directory initially contained data for more than 170 infectious agents from more than 40 government laboratories and linked to websites containing pertinent information about the agents and their associated diseases. During FY06, GEIS used supplemental funding for pandemic and avian influenza to increase coverage for influenza by incorporating influenza testing capabilities at 90 additional laboratories (military and state public health) in the directory. With this addition, data from more than 130 laboratories are available. Accessing the influenza material was refined by adding an “influenza data” link on the home page. Almost all state public health laboratories are participating in the influenza program in anticipation of a possible pandemic.

The directory website was visited more than 2,000 times in FY06. During domestic *Escherichia coli* outbreaks attributed to raw spinach consumption, the number of visitors increased significantly. The directory represents an important early step in the formation of a global military public health laboratory system.

### **Alert Component of DoD Medical Mortality Registry**

GEIS supports the Alert Component of the Mortality Surveillance Division of the Armed Forces Medical Examiner System at AFIP. The Alert Component actively monitors all active duty

deaths in real time for infectious or potentially infectious etiologies, notifies GEIS in the event of any clusters or unusual types of infections or presentations, and obtains specimens for more extensive testing and/or archiving whenever possible. This activity directly supports the GEIS pillar of surveillance by providing a means by which emerging infectious diseases can be detected.

The division strives to notify local preventive medicine and GEIS personnel of deaths that may require a public health response in a timely enough manner to ensure appropriate intervention. The Alert Component is a direct link between GEIS and AFIP for notification and investigation of deaths in military personnel that might be due to an infectious disease and therefore provides a mechanism for early warning of an outbreak.

Activities at the Alert Component consist of the following: 1) daily collection of mortality information from the Air Force, Army, Marine Corps, and Navy casualty offices, 2) collection of death circumstance information from DoD, federal, and civilian investigative agencies, and 3) regular contact with DoD and civilian medical examiners to obtain autopsy reports and to request specimen collection and agent-specific testing for infectious agents when appropriate. Copies of other related medical and personnel records may be requested to supplement the initial information. These records might include medical records from the individual’s base or hospital (at both residence and place of death), autopsy reports, AFIP consultations and toxicology studies, personnel records, legal investigations, safety and other special investigations, and eyewitness accounts. A physician individually reviews all complex cases to validate the medical cause of death. Once gathered and analyzed, the information is provided to various agencies and DoD leadership who can then use it to change policy and procedure based on objective evidence.

The goal for each active duty case is to obtain as complete a file as necessary to determine the medical cause of death. As it is obtained, information is reviewed to extract the relevant medical diagnostic material, risk factors, and circumstances of death, all of which are entered into the DoD

Medical Mortality Registry, a searchable database. The cause of death, co-morbid conditions, and ancillary and risk factors are coded and standardized using the *International Classification of Diseases*, 10th Revision. In addition to information on each death, up-to-date military personnel information is obtained from the Defense Manpower Data Center, and deployment history is obtained from its contingency tracking system. In cases of suicide, homicide, and potentially infectious disease in which travel history is relevant, deployment history is determined telephonically with the unit.

GEIS now has fully integrated the mortality registry database into the Armed Forces Medical Examiner Tracking System (AFMETS), which provides a valuable mechanism for historical analysis of suspicious deaths. This expansion supports the GEIS pillars of integration and cooperation by increasing the benefits of the database beyond the goals of the Alert Component. The database and system continue to develop in the number and type of variables, the number of cases, and, most importantly, the process.

The Alert Component has been receiving daily reports from the Army casualty office since late calendar year 2000 and began receiving daily e-mailed or faxed reports from each of the other three service casualty offices in January 2002. As of 24 October 2006, the DoD Medical Mortality Registry had 11,998 records from all services dating to October 1997. AFMETS directly imports several types of casualty data from the Defense Casualty Information Processing System to populate baseline demographic and incident information.

Although AFMETS is designed to be an operational tool for DoD medical examiners, it has become the centralized location for storing all casualty documentation in the Armed Forces Medical Examiner System. This includes, but is not limited to, autopsy reports, overseas death certificates (DD 2064), toxicology, and DNA reports. AFMETS is greatly enhancing the ability of the Mortality Surveillance Division to perform real-time surveillance, and as this tool develops it will become increasingly valuable to GEIS for identifying cases of infectious disease. Because AFMETS is web-based, military medical examiners worldwide can access it, and most military autopsy reports are directly uploaded into the system.

During FY06, 1,883 active duty fatalities occurred (Table 2), which, although down from FY05, nearly doubled the average annual number of deaths from 1998 to 2002. Combat deaths from Iraq and Afghanistan in FY06 accounted for 38 % of all active duty deaths and are responsible for most of the increase in total deaths. Accidental deaths comprise the other increase, which follows an overall increase in the number of aviation and motor vehicle crashes. GEIS received reports of 446 “illness” or “determination pending” deaths during FY06. All these cases were reviewed for a possible infectious disease cause. Of these 446 cases, 36 merited a more in-depth review, and 17 were determined to have an infectious disease cause with no underlying immunocompromise (Table 3).

GEIS thoroughly pursued the cause of each death that might have been caused by infectious disease. NHRC Respiratory Disease Laboratory scientists

**Table 2. Active Duty and Reserve Component Deaths by Manner, FY06**

Branch	Accident	Combat	Homicide	Natural	Suicide	Undetermined	Pending*	Total
Air Force	76	5	5	62	43	6	8	205
Army	267	491	23	137	94	16	22	1,050
Marines	121	195	8	10	20	1	12	367
Navy	120	16	8	46	32	4	35	261
Total	584	707	44	255	189	27	77	1,883

\*The relatively large number of pending cases reflects the end of FY report deadline: toxicological testing takes 6–8 weeks in most civilian laboratories.



**Table 3. Number of Active Duty Deaths Caused by Infectious Agents, FY06**

Disease category	Total deaths	Agent found	Primary cause of death
Respiratory	4	3*	Pneumonia
ARDS	1	0	ARDS
Myocarditis	2	1	Eosinophilic postvaccinia and influenza vaccines
Meningitis/encephalitis	3	2†	Meningitis ( <i>n</i> = 2), encephalitis ( <i>n</i> = 1)
Septicemia	4	4§	Sepsis ( <i>n</i> = 3), toxic shock syndrome ( <i>n</i> = 1)
Blood borne	1	1	Hepatitis C liver failure
Pending	2	—	—
Total	17	11	

\* *Streptococcus pneumoniae*, group A *Streptococcus*, Hantavirus.

† Group A *Streptococcus*, pending testing.

§ *Staphylococcus aureus* (*n* = 3), *Neisseria* (*n* = 1).

were consulted in all cases of respiratory disease for which a pathogen was not identified at or before autopsy, and isolates of the group A *Streptococcus* were sent to NHRC for further characterization. Staff of AFIP infectious disease, pulmonary and cardiovascular branches was extensively consulted as part of the process of identifying an infectious etiology when the cause of death was not apparent. Finally, USAMRIID was consulted for Hantavirus testing, and the Vaccine Healthcare Center and the University of Washington were consulted for the postvaccinia and influenza vaccine myocarditis cases.

Reports consist of routine monthly mortality with summary analysis to Air Force, Army, and Navy medical leadership. These reports are used to monitor major categories of death in real time and allow response when indicated. In addition, AFIP notifies GEIS via e-mail of any infectious or potentially infectious deaths and when deaths exceed expected levels; cases are reported in the biweekly GEIS teleconferences.

Daily active surveillance of all deaths has led to a process by which the Armed Forces Medical Examiner, the chief of operations, and the investigative staff are notified of all deaths in a timely manner, without relying on contact by field agents. The result has been a more active role of the armed forces medical examiners in all cases, sometimes to the point of transferring the body from a civilian

facility to a military one for autopsy. The benefit to DoD is that all active duty deaths are now investigated, leading to a full accounting of cause of death. GEIS benefits in that all armed forces medical examiners are aware of the GEIS concern over vaccine-preventable, emerging, and potentially unnatural infections. All such cases are now routinely brought to the immediate attention of GEIS. The armed forces medical examiners have changed their practice to include saving fresh frozen lung tissue and blood on cases that have an unclear or infectious cause of death to facilitate PCR testing. Finally, they are far more likely to send specimens from suspected infectious disease deaths for further microbiological and molecular testing than their civilian counterparts.

The Mortality Surveillance Division is the only centralized agency in DoD with the mission and authority to investigate the medical cause of death for all active duty personnel. Other DoD agencies, such as safety centers and casualty offices, are service-specific and have information on only a portion of active duty deaths. The medical information obtained by Mortality Surveillance Division is used to accurately and specifically determine why young, presumably healthy, servicemembers die. Similarly, in a mass casualty event the Mortality Surveillance Division is the only DoD agency with the authority, experience, and capability to accurately track the medical cause of death, as determined by autopsy results.

As a key sponsor of the Mortality Surveillance Division, GEIS provides the foundation for the Alert Component, as intended, and for the overall division. The program has grown from the roots furnished by GEIS, but surveillance for emerging infections remains, and shall continue to remain, the core of its activities. The direct connection

between GEIS and the AFIP Mortality Surveillance Division provides the unique DoD-level link between military infectious disease mortality notification/investigation and GEIS, the sole organization within DoD that is responsible for identification of emerging infectious diseases that might threaten US military and civilian populations.

### *Pacific Air Forces*

Through the congressional supplemental funding for pandemic and avian influenza, GEIS and the Pacific Air Forces trained military and civilian health professionals throughout the Asia-Pacific region in rapid response to avian and pandemic influenza. This activity built capacity for cohesive, synchronized preparedness and response efforts in support of PACOM, DoD, and US national and international pandemic influenza preparedness plans.

GEIS supported the Pacific Air Forces to enhance outbreak preparedness and response capability among military and civilian personnel in collaboration with the CDC and in accordance with WHO rapid response and containment initiatives (WHO pandemic influenza draft protocol for rapid response and containment, May 2006). The project grew from a CDC train-the-trainer rapid response team workshop in Bangkok in July 2006, in which DoD representatives participated. This training program, conceived by WHO and CDC, was the first of its kind. The international training was designed to provide a global, standardized framework for immediate national responses to an emergence of a pandemic influenza strain. The response would be based on common public health investigation and control measures and scientific knowledge but would follow an approach that is to be adapted before a pandemic by relevant public health authorities locally and regionally.

Three separate training activities were executed in FY06, one each in Hawaii, Malaysia, and Cambodia.

*Hawaii.* Nearly 60 public health emergency officers and other public health officers from all service components and civilian counterparts became familiar with the WHO

strategies for rapid response to pandemic influenza. Triservice and multiagency representation fostered collaboration within the state in pandemic influenza preparedness efforts, supporting the GEIS goal of cooperation and capacity building.

*Malaysia.* Fifty-five personnel from the Ministry of Health, Ministry of Defense, private hospitals, and US embassy participated in this “train the trainers” workshop on WHO strategies for rapid response to pandemic influenza. The Malaysian Ministry of Health and Ministry of Defense established a relationship for coordination; NAMRU-2 and the Ministry of Health initiated a partnership to develop a health surveillance network; and a multilateral regional biosecurity workshop was planned for April 2007. After the workshop, the Honorable Christopher LaFleur, US ambassador to Malaysia, stated that this Pacific Air Forces activity “was well received and valued by the Malaysian participants” and that “...this training was beneficial in enhancing Malaysia’s capabilities in responding to the threat of Pandemic Influenza.”

*Cambodia.* A subject matter expert exchange led to interagency collaboration for planned rapid response training for the Royal Cambodian Armed Forces, Royal Cambodian Armed Forces health surveillance initiatives, nonpharmacologic intervention and capacity building, a PACOM-funded follow-up subject matter expert exchange in October 2006, a rapid response workshop in January 2007, and planned continued collaborations, including health surveillance efforts.

In the subject matter expert exchange, PACOM connected with the Department of State, USAID, and the CDC to define the role of DoD in the inter-agency support to Cambodia. PACOM and GEIS funded personnel to return to Phnom Penh in October 2006 to conduct a follow-on activity and participate in the first Cambodian Ministry of Health rapid response train-the-trainer workshop for the Royal Cambodian Armed Forces. Equipment has been purchased to initiate Royal Cambodian Armed Forces health surveillance activities and develop strategies to enhance infectious control measures in military health care facilities.

The breadth of interagency and international cooperation involved was demonstrated by the range of participants: PACOM, two DoD overseas laboratories (AFRIMS and NAMRU-2), ministries of health, local developmental organizations (e.g., USAID and the United Nations Development Programme), a US embassy, and representatives from the People's Republic of China military.

Common approaches to preparedness were ensured, along with effective response to disease outbreak, including early containment of potential influenza and other emerging infectious agents. Military-to-military relationships were enhanced, and host nation military capacity to respond to disease outbreak and to assist host nation civilian organizations was improved.

Topics in the training included investigation and control of avian influenza infection in poultry, case management of suspect human avian influenza infection, laboratory diagnostics, specimen collection and biosafety, personal protective equipment, emergency public health messages during a pandemic, and interventions to contain a pandemic. In addition to the CDC modules, Pacific Air Forces/PACOM adapted the training to address military needs (which were not covered by the CDC material) by developing health surveillance capability and reporting procedures, military-specific preparedness and response activities, and military assistance to civilians.

Objectives of the training were 1) to ensure a cohesive rapid response approach to potential disease

outbreak through full coordination and collaboration with other DoD organizations, CDC, WHO, USAID, and nongovernmental and international organizations; 2) to intensify collaboration between US and host nation military, civilian health sectors, and nongovernmental organizations; 3) to strengthen rapid response training to rural residents; and 4) to improve effective approaches to early containment of influenza outbreak.

The outcome should enhance host country capability to mitigate the spread of a potential deadly influenza outbreak and provide future partners in medical information exchange. This initiative directly benefits nonwarfighting operations and meets PACOM engagement intent to strengthen ties and build host nation capacity. The US military benefits from better understanding of host nation health surveillance infrastructure and outbreak response capacity. Improving host nation ability to contain or delay spread at the source would limit the spread of disease to US military personnel, both OCONUS and CONUS. The training also provided a forum for military medical professionals to discuss concerns related to pandemic influenza and joint research initiatives to guide prevention and response.

Taken together, these activities conducted with GEIS funding have supported the DoD Pandemic Influenza Implementation Plan (August 2006) with the intent of 1) stopping, slowing, or otherwise limiting the spread of a pandemic to the United States; 2) limiting the domestic spread of a pandemic and mitigating disease, suffering, and death; and 3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. Specifically, the Pacific Air Forces project has directly supported four of the thirteen priority action areas for which DoD has primary responsibilities within the national plan for pandemic influenza: advance international cooperation, build international capacity, ensure rapid response, and provide early warning. GEIS plans to expand the training program within Cambodia and to add courses or workshops in countries within the PACOM area of responsibility, to include India, Lao PDR, Indonesia, the People's Republic of China, and Vietnam.

## *DoD Veterinary Service Activity*

The response to an outbreak of avian influenza in the United States would of necessity simultaneously involve government, military, industry, and academia. In recognition of the challenges and to broaden understanding of this grave prospect, GEIS and the DoD Veterinary Service Activity (DoDVSA) in the Office of the Army Surgeon General coordinated a meeting of veterinary and medical officials who would be involved in such a response. This Avian Influenza Surveillance Workshop was held 29–31 August 2006 in Crystal City, Virginia.

More than 70 attendees grappled with the issues anticipated in the event of a highly pathogenic avian influenza H5N1 strain entering the United States. The participants at this unprecedented gathering included the Deputy Assistant Secretary of Defense for Force Health Protection and Readiness; the USACHPPM Commander; leaders from

USDA, Homeland Security, Department of the Interior, Department of State; and the GEIS Director. The roles and capabilities of the agencies in the event of an outbreak were clarified. Topics among the 32 presentations included commercial poultry programs, the animal-human interface, homeland security, surveillance collection, and laboratory logistics.

Possible solutions were discussed in breakout sessions and informally. New points of contact were made, and a comprehensive e-mail roster of attendees was sent to all that attended. The presentations were posted on the DoDVSA website and are available on request from DoDVSA. The breakout groups examined four activities: surveillance collection, surveillance analysis, laboratory work, and risk communications. Results of the workshop breakout groups are being processed.

## *United States Army Center for Health Promotion and Preventive Medicine*

### **Health Risk Communication Training**

After creating a website to solicit input from public health practitioners about training needed to prepare for an influenza pandemic, GEIS and the US Army Center for Health Promotion and Preventive Medicine (USACHPPM) developed an exportable risk communication training program for DoD personnel. This training will be provided to public health emergency officers over the coming year.

### **Epidemiologic Investigations**

In its designated operational role, USACHPPM performed several infectious disease outbreak investigations. Information relating to these investigations was presented and discussed in the biweekly epi-chiefs teleconferences. Two of these investigations were formal epidemiology consultations (EPICONS) tasked through the Army Surgeon General, and both benefited from cross-service informal sharing of information that occurred during the GEIS-hosted epi-chiefs teleconferences.

### **Analysis of Deployment Health Surveillance Data**

Through a project sponsored by GEIS and USACHPPM, health outcomes during Operation Enduring Freedom and Operation Iraqi Freedom in the CENTCOM area of responsibility were assessed. Medical conditions that resulted in a documented hospitalization at an Army combat support hospital or an air medical evacuation to a EUCOM or CONUS level IV or V treatment facility were tracked (Figure 10). Data sources included the Patient Administration Systems and Biostatistical Activity standard inpatient data records for level III facilities in theater (i.e., SIDR-III), the TRANSCOM Regulating and Command and Control Evacuation System (TRAC<sup>2</sup>ES), and the Defense Manpower Data Center deployment rosters. The primary objective was to determine the potential burden of disease and probable risk factors associated with ongoing CENTCOM operations.





Figure 10: 228th Combat Support Hospital in Mosul, Iraq.

A more thorough understanding of available data sources was crucial, because multiple health surveillance systems and reporting tools are used in theater and because the quality and completeness of the data can vary significantly for each method as well as by military service, reporting units (i.e., line or medical), and echelon of care. Therefore, a secondary goal of the analysis was to provide an overview of in-theater surveillance capabilities that included ad hoc query results from deployment health surveillance systems and disease and nonbattle injury summary reports.

During this process, weaknesses in reportable medical event capture occurring in theater were discovered and documented. Medical events are currently reported from deployed medical units via the Joint Medical Workstation (JMEWS) through the Secure Internet Protocol Router Networks; there they reside as an archived library with no analytic functionality and with restricted access. To address these limitations, JMEWS has mapped electronic patient encounter module data diagnosis codes to identify reportable medical events. However, inpatient data and deployment health information gained from additional surveillance systems are largely excluded, and data reside on a classified network that hinders extraction of individual records to allow linkage with other systems. Analysts explored unclassified health outcomes data not included in JMEWS by mapping diagnostic codes from hospitalization records (SIDR-III), medical evacuations (TRAC<sup>2</sup>ES), and patient encounters tracked through the Joint Patient Tracking Application (JPTA).

Each stage of the analysis demonstrated gaps in data acquisition among sources and the need for consolidated health surveillance data to obtain

**Table 4. Top Three Deployment-related Reportable Medical Events as Determined by Review of SIDR-III, TRAC<sup>2</sup>ES, and JPTA**

Reportable medical event		Frequency			Consolidated <sup>1</sup>	
Name	ICD-9 code	SIDR-III	TRAC <sup>2</sup> ES	JPTA	Frequency	%
<b>1. Leishmaniasis (all)</b>		<b>77</b>	<b>409</b>	<b>237</b>	<b>458</b>	<b>75.7</b>
Unspecified	085.9	77	201	117	214	35.4
Cutaneous, Asian desert	085.2	0	138	97	169	27.9
Cutaneous	085.4	0	59	19	62	10.2
Cutaneous, urban	085.1	0	10	4	13	2.1
Visceral	085.0	0	1	0	1	0.2
Mucocutaneous	085.5	0	0	0	1	0.2
<b>2. Malaria (all)</b>		<b>57</b>	<b>22</b>	<b>38</b>	<b>71</b>	<b>11.7</b>
Unspecified	084.6	38	11	24	39	6.4
Other	084.4	2	3	13	14	2.3
Vivax	084.1	9	2	1	9	1.5
Falciparum	084.0	7	5	0	8	1.3
Malariae	084.2	1	0	0	1	0.2
Other pernicious complications	084.9	0	1	0	0	0.0
<b>3. Heat stroke/exhaustion</b>		<b>38</b>	<b>1</b>	<b>1</b>	<b>39</b>	<b>6.4</b>
<b>Total</b>		<b>172</b>	<b>432</b>	<b>276</b>	<b>568</b>	<b>93.9</b>

Data represent primary and secondary diagnoses from 1 October 2001 to 31 December 2005 ( $n = 605$ ).

<sup>1</sup> Consolidated results are based on an integration of SIDR-III, TRAC<sup>2</sup>ES, and JPTA data; duplicate records were excluded so that only the most specific diagnosis code entered per reportable medical event was retained.

more complete and reliable analyses of health outcomes occurring in theater. For example, a review of SIDR-III, TRAC<sup>2</sup>ES, and JPTA to assess deployment-related reportable medical events revealed that each source contributed to reportable medical event case identification (Table 4). Although substantial improvements in data capture are occurring, individual sources remain incomplete, and summary reports describing this sort of consolidated data analysis are lacking. The analysis also revealed significant differences in reported health outcomes, including reportable medical events between demographic groups that should be substantiated with more complete data. For example, soldiers had more documented hospitalizations, medical evacuations, and reportable medical events than other servicemembers, which may indicate occupational or exposure differences that should be explored further.

### Serosurveillance for Avian and Pandemic Influenza Utilizing DoD Serum Repository

The serum specimens contained within the DoD Serum Repository provide a unique opportunity to generate seroepidemiologic data to enable surveillance for H5N1 and related avian and pandemic influenza virus exposure and to permit rational vaccine or therapeutic selection in the event of an outbreak. In FY06, work was initiated to develop a Center for Epidemiology and Serosurveillance of Pandemic Influenza, the primary objectives of which included 1) assessing the prevalence of exposure to avian influenza strains among military servicemembers, 2) providing serologic data to support investigations of geographically localized avian and pandemic influenza outbreaks, and 3) investigating the prevalence of a preexisting antibody against human influenza strains that may provide the potential for cross-reactive protection from avian influenza infection among servicemembers in the event of an avian and pandemic influenza outbreak.

Progress has been made in meeting these objectives. Additional staff have been hired to implement and oversee the project. Detailed programs have been generated to identify servicemembers deployed to or living in areas of H5N1 activity through the Defense Medical Surveillance System. Southern Research Institute (Birmingham, AL) has been identified as a qualified and experienced laboratory

that will perform both avian (H5N1 clades 1 and 2 subtypes) and human influenza (H3N2 and H1N1) seroprevalence testing of DoD Serum Repository specimens through the use of hemagglutination inhibition assays with confirmatory microneutralization assays. An initial volume of 3,000 specimens has been agreed upon for testing [2,000 serum specimens (pre- and postdeployment) from servicemembers deployed to or living in Thailand, Indonesia, and Vietnam and 1,000 serum specimens from recruits entering military service in 2005]. Initial testing is to begin in February 2007, with final results of all assays received by the end of April 2007.

### Pandemic Influenza Workshop, Force Health Protection Conference

A training course aimed at improving preparedness and response to an influenza pandemic was held 7–8 August 2006 in Albuquerque, New Mexico. The course was a collaborative effort between USACHPPM and GEIS Headquarters and was supported by the supplemental funding for pandemic and avian influenza.

The target audience comprised military public health emergency officers and other public health practitioners. More than 300 participants from the Army, Navy, Air Force, Marines, and Coast Guard participated as well as personnel from other US government agencies, including the Departments of Veterans Affairs and Homeland Security and allied country militaries. The workshop covered lessons learned from previous pandemics and the swine influenza response in 1976, surveillance for influenza and emerging pathogens, and components of the national, DoD, COCOM, and US Army Medical Command efforts toward preparedness. In addition, other areas were discussed: community preparedness, incident command at the local level, pharmacological and nonpharmaceutical methods of preventing and slowing the spread of infection, triage and treatment options, use of personal protective equipment, legal considerations involved in responding to a pandemic, communications during a pandemic, and the management of mass fatalities. A highlight of this conference was the keynote address by John M. Barry, author of *The Great Influenza: The Epic Story of the Deadliest Plague in History* (New York: Penguin Group, 2004).

## *Analysis of Deployment Health Surveillance Data from Operation Iraqi Freedom and Operation Enduring Freedom*

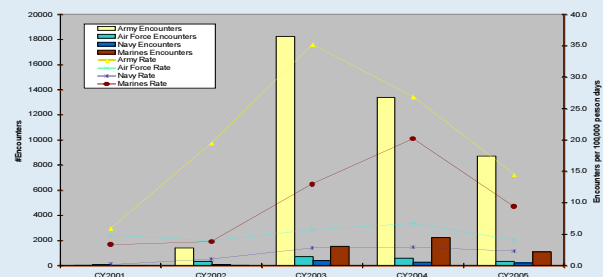
Casualty estimates for current operations in the CENTCOM area of responsibility, Operation Enduring Freedom and Operation Iraqi Freedom, are widely publicized. As of 28 September 2006, estimated US casualties, which are predominately due to traumatic or combat-related medical events, included 3,335 deaths and 21,425 wounded in action (<http://www.defenselink.mil/news/casualty.pdf>). Surveillance of such events is fairly accurate and complete because the severity of the injury typically necessitates removal from the theater of operation to secure, fixed medical facilities where health surveillance technology and reporting are well established.

In contrast, little is known about newly acquired or exacerbated medical conditions not directly caused by combat that occur to soldiers while in theater. Such conditions are referred to as disease nonbattle injury (DNBI). Historically, DNBI events have exceeded combat-related casualties and have significantly reduced the effectiveness of military units and affected the outcomes of military campaigns. The DNBI burden on combat readiness in Operation Iraqi Freedom and Operation Enduring Freedom has not been readily known. To establish this information, GEIS supported the first retrospective analysis of DNBI burden in Iraq and Afghanistan through a USACHPPM review of hospitalization and air medical evacuation data from the CENTCOM area of responsibility.



Medical evacuation mission along Turkish border.

GEIS found that because reportable medical event (RME) reports and laboratory confirmation within-theater are unavailable in a manageable electronic database, short-term solutions to extract cases from in-theater health surveillance systems and patient tracking applications are needed. JMEWS has created this functionality by developing ad hoc query capability for RMEs; however, the information resides on a classified network, and extracting individual records with full patient identifiers or SSNs to allow linkage with other systems is difficult. A review of the three systems used in this analysis (SIDR-III, TRAC<sup>2</sup>ES, and JPTA) revealed that each data source contributed to RME case identification. More complete capture of these probable RMEs will require merging with other sources such as JMEWS and other patient tracking applications. Although the data utilized for this analysis do not constitute a complete RME dataset, the available data demonstrate significant predictors of risk (e.g., Army membership, male gender, enlisted status, and active duty membership) that should be explored further with a more complete dataset. With this study, GEIS has established the baseline for health risks and DNBI in the CENTCOM area of responsibility and revealed the need for fundamental improvement in information management related to infectious disease surveillance.



Army combat support hospital encounters and air medical evacuations by service, 2001–2005. Encounters based on utilization of Army CSH (SIDR-III) or TRANSCOM air medical evacuation system (TRAC<sup>2</sup>ES).

## Standing Ready: The National Guard Response to Pandemic Influenza

The Army National Guard medical team held a training seminar for medical professionals aimed at improving preparation and response to an influenza pandemic. The seminar, entitled “Standing Ready: The National Guard Response to Pandemic Influenza,” was held in May 2006 in Dallas.

USACHPPM and GEIS Headquarters staff collaborated with the National Guard to facilitate the conference, which targeted National Guard medical team members, who are expected to be involved in the nation’s response to an influenza pandemic. The conference was attended by 180 registered participants, representing 53 of the 54 National Guard state and territorial units.

## United States Army Center for Health Promotion and Preventive Medicine-West

The United States Army Center for Health Promotion and Preventive Medicine-West (USACHPPM-West) conducted disease surveillance and public health capacity building in Guatemala, El Salvador, and Honduras as part of a multiyear effort begun with GEIS in 2002. The approach has been to identify human disease agents, reservoirs, and vectors that have an impact on public health in the communities served by the host country ministries of health (MOH). Methods and technology that could be assimilated into existing surveillance programs were exported to the host countries.

The purpose of this effort has been to improve the public health infrastructure in Central America with adaptable, sustainable systems that can be easily maintained at the local level, directly supporting the GEIS pillars of capacity building and surveillance. In addition, SOUTHCOM contributed to the funding, underscoring the importance of the work to both GEIS and the COCOM missions.

Investigators have documented outbreaks of Venezuelan equine encephalitis, Eastern equine encephalitis, and Patois and Nepuyo viruses in Central America along with the reemergence of dengue in the last few decades. It is almost certain that many other arboviruses are circulating given the diversity and density of arthropod species and zoonotic hosts in the regions. There is evidence that vector- and rodent-borne bacterial agents are causing significant febrile illnesses in Central America. USACHPPM-West investigators have detected antibodies for spotted fever group *Rickettsia*, typhus group *Rickettsia*, ehrlichiosis, or

leptospirosis in febrile patients from Honduras and El Salvador, with seroprevalence as high as 20 % in selected communities. Currently, MOH laboratories in Central America operate disease surveillance programs for some of these pathogens but cannot assay for most arboviruses, *Rickettsia*, and *Ehrlichia* agents. Furthermore, respiratory infections are among the most frequently reported illnesses in Central America, especially in children and the elderly, and are a leading cause of mortality in both groups. MOH laboratory personnel in the region are initiating surveillance activities for viral agents that cause respiratory illnesses and will use serological assays to evaluate specimens in accordance with the Pan American Health Organization guidelines.

Scientists from USACHPPM-West and collaborating DoD laboratories assisted MOH authorities in conducting disease surveillance activities in Honduras, El Salvador, and Guatemala. These efforts centered on building capabilities at host country public health laboratories to enable MOH personnel to more independently monitor infectious diseases. Specific activities included transfer of equipment, supplies, and reagents to the MOH that were not readily available in the host countries. DoD subject matter experts provided instruction on the use of this equipment and reagents and advised public health workers on various issues concerning disease surveillance and laboratory operations. USACHPPM-West scientists trained MOH physicians, veterinarians, and public health workers in surveillance and laboratory analysis of rodents for pathogenic agents.



DoD personnel also helped Honduran medical authorities establish several sentinel sites to collect human samples for influenza surveillance. Investigators selected distant locations (e.g., rural areas) where MOH medical personnel experienced difficulties in conducting a successful surveillance program. These remote sites represent areas in Central America that are experiencing an increasing influx of people from Asia who bring diseases from Asia into the region. Accordingly, surveillance data generated from these sites may help provide early warning of pandemic influenza spreading into the Western Hemisphere. MOH medical personnel collected nasal swab specimens at these sites and shipped the specimens to the AFIOH for evaluation using standard protocols. MOH personnel from Guatemala also shipped specimens to AFIOH for evaluation by isolation and to USACHPPM-West for molecular analysis using RT-PCR. USACHPPM-West technicians shipped aliquots of RT-PCR positive specimens to AFIOH for sequencing and inclusion into AFIOH surveillance databases. The interaction of AFIOH with USACHPPM-West helped broaden and strengthen the GEIS-supported Global Influenza Surveillance Program by providing specimens with unique origins from Central America.

MOH authorities from Guatemala, Honduras, and El Salvador shipped specimens from febrile patients without influenza-like illness syndromes to

USACHPPM-West in FY06 for evaluation with methods that are unavailable in the host countries. Dengue was the most frequently detected pathogen in febrile illness patients, with investigators successfully amplifying dengue serotypes 1, 2, and 4 with RT-PCR. Laboratory personnel continued to detect enteroviruses in individuals suffering from aseptic encephalitis and meningitis. In FY06, investigators evaluated tissue specimens for leishmaniasis parasites by PCR and are now developing protocols to identify the specific parasites indicated by the screening process.

Through the GEIS-supported efforts of USACHPPM-West and its collaborators, public health personnel in Honduras, El Salvador, and Guatemala could successfully establish a new sustainable surveillance program to detect and analyze diseases of public health importance. Health authorities in the host countries are using results from the investigations to reprioritize the use of limited resources in the fight to control infectious disease. DoD preventive medicine specialists use the information to protect US military personnel who deploy to Central America each year. By cosupporting the infectious disease surveillance performed by USACHPPM-West and GEIS, SOUTHCOM has recognized this work as essential to the SOUTHCOM mission.

## *Navy Environmental Health Center*

### **Population Health Directorate**

The Navy Environmental Health Center (NEHC), the medical surveillance hub of the Navy, strengthened the GEIS pillars of surveillance, response, and innovation by improving MHS surveillance capacity in FY06. Four years of ongoing development, including the Health Level Seven (HL7) electronic medical data validation project with the Executive Information and Decision Support Program Office, positioned NEHC to deliver capability for a functional MHS electronic laboratory. NEHC employed this HL7 data surveillance capability in FY06 to

support critical Force Health Protection management decisions at all levels within DoD. In addition, NEHC began validating HL7 pharmacy and radiology data for medical surveillance utility.

Confronted by emerging global disease threats, the public health profession must rapidly characterize exigent conditions to facilitate development of containment measures in a resource-limited setting. MHS medical surveillance is predominantly issue-based, comprising 1) passive surveillance of more than 70 reportable events, 2) laboratory surveillance of acute respiratory infections among

## HL7 Standard Used for Military Surveillance

NEHC has long been a leader in the electronic capture of data for medical surveillance. In FY06, GEIS and NEHC continued to develop and test methods to use electronic messages conforming to the Health Level Seven (HL7) standard from the CHCS for laboratory reporting of key infectious diseases and to assist with case finding for public health professionals. CHCS is an electronic system used in MTFs to track services related to patient encounters, including outpatient visits, clinic appointments, pharmacy orders and fills, radiology examinations, laboratory test orders and results, and inpatient admissions and discharges. More than 100 CHCS servers distributed worldwide support MTFs in a particular geographic area. However, each CHCS is isolated and cannot communicate with another. Therefore, global collection of laboratory reports from CHCS systems has been a challenge.

HL7 is a national standard messaging format used by health care systems to exchange data (including laboratory results) in support of clinical patient care and health care services. In the MHS, administrative and ancillary services (laboratory, pharmacy, and radiology) associated with inpatient and outpatient visits are electronically tracked in CHCS. Furthermore, each CHCS is programmed to send HL7 messages. In CHCS, an HL7 message is triggered when a laboratory result is certified, a medication label is printed, or a radiology report is verified.

An MHS data repository receives HL7 laboratory results from CHCS in real time. With GEIS support, NEHC now ensures that these messages are parsed into a database. The message parsing process and database design have been refined and standardized. As a result, these data are used to support critical preventive medicine efforts and programs. In FY06, these data supported deployment health concerns associated with drug-resistant *Acinetobacter baumannii* infections in the Iraq theater and provided case findings within a few hours in support of a multistate outbreak of *Fusarium keratitis* linked to a commercial ophthalmic solution.

### Case Finding for Public Health Concerns

#### *Fusarium keratitis*

14 positive *Fusarium* cultures grown from ocular specimens or specimens associated with contact lenses.

Seven unique individuals, three of which had date of specimen collection since October 2005.

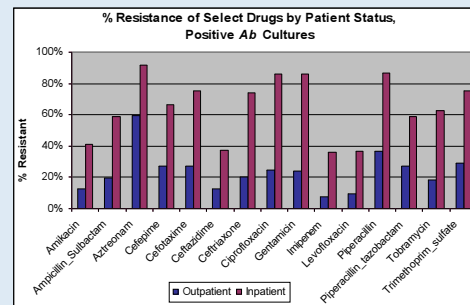
Information on all three individuals sent to local hospital via service surveillance hub.

One case reported to CDC as a possible case associated with public health alert and meeting case reporting criteria.

HL7 database was used to identify previously unidentified *Fusarium keratitis* in a multistate outbreak.

### Surveillance of Antibiotic Resistance

*Acinetobacter baumannii*, May 2004–January 2006



*A. baumannii* antibiotic resistance profiles from multiple MTFs over 20 months, data that clearly enhance MHS situational awareness about this emerging infectious agent.

recruits, 3) antimalarial resistance surveillance, 4) surveillance of circulating influenza strains, 5) surveillance for deployment-related mental health conditions, and 6) syndromic surveillance of clinic visits among MHS fixed treatment facilities. The military is poised, therefore, to address many public health threats. However, despite the robust MHS

effort, flexibility is needed because the optimal approach to early threat detection depends on the disease, and significant gaps exist in the military's cache of surveillance programs. To address a broader range of preventive medicine needs, particularly given the challenges presented by unanticipated operational exposures, opportunistic

data must be mobilized. These data, including clinical laboratory, pharmacy, and radiology records, are already collected electronically in a central MHS location.

GEIS supported the NEHC central collection of clinical data for surveillance use. This support enabled the creation and maintenance of a viable electronic laboratory database containing clinical laboratory results of all chemistry, microbiology, and anatomic pathology tests run in a fixed military treatment facility (MTF). Because these datasets are large, GEIS and NEHC developed a strong information management/information technology infrastructure in FY06 to promote timelier trend analysis. In support of DoD pandemic influenza surveillance efforts, NEHC received daily laboratory data feeds on all DoD beneficiaries. Data collected regularly since May 2004 are organized into three data tables: chemistry, microbiology, and anatomic pathology. NEHC has developed methods to accommodate nonstandardized data fields, including laboratory test name and specimen type.

Ongoing work is establishing the strengths, limitations, completeness, and scientific value of these data. Elements essential for medical surveillance and response (e.g., test name, test result, and MTF) are included with few missing entries. Data tables can be queried for disease outcome and other factors including MTF, duty status, and service. Patient status can be determined as outpatient or inpatient, and most results can be interpreted by local MTF reference ranges. Infectious diseases of public health concern for which laboratory test results are cached include malaria, tuberculosis, meningococcal meningitis, dengue, and leishmaniasis.

Data limitations were identified and included the following: 1) test names and results are nonstandardized; 2) laboratory records reflect those entered in the local Composite Health Care System (CHCS); 3) results for specimens collected and tested at laboratories not affiliated with the MTF are not included; and, 4) results for specimens collected by the MTFs but referred for outside laboratory testing may not be entered into the CHCS. After identifying these limitations to ensure transparent and accurate analysis, the fundamental HL7 data strengths emerged. These data clearly comprise the

sole useable, timely, and centrally located laboratory results for the MHS. HL7 results present significant value to MHS leaders who rely on data-driven decision making to address pressing military public health concerns.

Throughout FY06, laboratory results were used to support preventive medicine inquiries and investigations at all surveillance and response levels. Requests for information came from multiple commands, including the Navy Bureau of Medicine and Surgery, MTFs, and GEIS partners. The conditions that triggered the requests were possible tuberculosis, suspected Q fever, group A beta-hemolytic streptococcus, sickle cell anemia, G6PD deficiency, West Nile virus, pediatric blood lead levels, legionellosis, coccidioidomycosis, *Fusarium* species eye infections, mumps, dengue, *Acinetobacter baumannii* drug resistance, and chlamydia screening. Answers for urgent data calls were provided within two working days, except for antibiotic resistance information, which took up to 3 weeks of dedicated work time to provide.

In addition to laboratory results, NEHC began assessing HL7 radiology reports and pharmacy transactions in support of GEIS and DoD-Health Affairs to improve pandemic influenza surveillance. Methods were established to track influenza via laboratory data, and the usefulness of pharmacy and radiology HL7 data in surveillance was assessed given that electronic HL7 radiology reports have never been evaluated for surveillance use. Initial DoD work on employing pharmacy data for surveillance halted after the 2005 transfer of the ESSENCE epidemiology syndromic surveillance work away from WRAIR. The ESSENCE preliminary studies on the use of pharmacy transactions to track respiratory illness outbreaks were encouraging.

Preliminary NEHC assessments indicate that HL7 pharmacy transactions can add great value to surveillance. A separate DoD data stream of pharmacy orders, the Pharmacy Data Transaction Service, is well-known and currently used by the Pharmacoeconomic Center and ESSENCE for clinical epidemiology and surveillance. Data from this stream include all outpatient pharmacy transactions occurring in the direct care setting or billed to the MHS (prescriptions filled outside the MTF and via

the mail order pharmacy) but do not include inpatient transactions. In contrast, the HL7 pharmacy data include all direct care pharmacy transactions, both outpatient and inpatient, but similarly do not include pharmacy transactions occurring outside the MTF or via mail order. Initial assessment of the HL7 pharmacy outpatient transactions indicates high data quality. Most major MTFs were represented in the data.

HL7 data provide a unique capability given the established expertise of NEHC in mining these novel data streams that represent the only near real-time laboratory and radiology data centrally available within the MHS. Judicious exploitation of these clinical data will undergird an MHS strategy that detects and monitors emerging infections, the diseases they cause, and the factors influencing their emergence. These efforts will directly advance the GEIS emerging infections surveillance and response mission.

### *Navy Investigates Pervasive Infection in Pacific Submarine Force*



Infection of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has been problematic during FY06 for training and deployed forces and has resulted in lost duty hours and reduced force readiness. One deployed population affected by CA-MRSA in FY06 was the Pacific Submarine Force (SUBPAC).

The skin and soft tissue infections caused by this bacteria are a high threat to these assets because sailors aboard submarines live in crowded quarters for 6 months, so the likelihood of person-to-person transmission is high. In addition, the organisms are resistant to multiple antibiotics, and submarine medical personnel may not be prepared to recognize and/or treat CA-MRSA disease. Infected crewmembers may require

removal while the submarine is underway to prevent spread to other crewmembers and to receive adequate treatment. The presence of CA-MRSA cannot be reliably predicted from clinical or historical features, so clinicians must rely on ancillary testing and an understanding of local resistance patterns.

Awareness of ongoing CA-MRSA infections and concern about the consequences of an outbreak became severe enough in FY06 for the SUBPAC commander to commission an outbreak investigation and force-wide survey, which were conducted by Navy Environmental and Preventive Medicine Unit Six (NEPMU6) from Hawaii with GEIS support. Subjects were 840 recently deployed submarine crewmembers who completed questionnaires and gave nasal swab samples that were analyzed for subclinical carriage of MRSA. The study covered eight Los Angeles class attack boats and found an average 1.4% nasal carriage rate for CA-MRSA bacteria among the submariners. This carriage rate is similar to that in the civilian population. However, two submarines taking part in the study had approximately double carriage rate for MRSA. In the submarines with increased rates, slightly increased risk of CA-MRSA carriage was associated in sonar technicians and those working in navigation areas of the boat. Although all isolates were resistant to multiple antibiotics, all were susceptible to trimethoprim-sulfamethoxazole for treatment.

NEPMU6 recommended that Independent Duty Corpsmen, the health care providers aboard submarines, be provided training and supplies to identify and treat CA-MRSA infections while the submarines are deployed. This actionable information gained from the NEPMU6 study reduces the threat posed to these forces by CA-MRSA and therefore helps maintain operational readiness in this force asset that is critical to national defense.



## **Navy Environmental and Preventive Medicine Unit No. 7 (NEPMU7)**

Through GEIS support, Navy Environmental and Preventive Medicine Unit No. 7 (NEPMU7), located in Sicily enhanced febrile respiratory disease surveillance, particularly for influenza, in the EUCOM and CENTCOM areas of operation. The GEIS influenza surveillance program is essential for the early detection and identification of emerging respiratory pathogens at DoD facilities worldwide. Navy MTFs and Army forward-deployed troop medical clinics throughout the EUCOM and CENTCOM regions are strategic elements in emerging infectious disease surveillance and represent opportunities for enhancing the existing respiratory disease surveillance efforts of GEIS.

The primary objectives were to increase the number of sentinel sites and increase specimen submissions from established sites to the GEIS influenza surveillance laboratory hub at AFIOH, with a particular focus on forward-deployed locations in the CENTCOM area of operations. The secondary objectives were to enhance regional surveillance partnerships, to increase the number of military medical personnel trained in respiratory disease surveillance, and to improve surveillance efforts in areas of strategic importance.

New sentinel sites were proposed based on geographic location, number of troops served, and available local capacity. Communications with and briefings to the command medical decision-makers were used to build command support for implementation of the GEIS-supported Global Influenza Surveillance Program at each medical facility. A surveillance champion was identified at each new

and existing sentinel site that agreed to participate during the 2005–2006 influenza season. Site visits were conducted to educate and train the designated local surveillance champion, command decision-makers, medical staff, and laboratory staff. In addition, initial supplies were provided, and the logistics of specimen collection, storage, and shipping were developed for each facility during the site visits. Ongoing consultative support, program assistance, and surveillance data were provided.

Two existing CENTCOM forward-deployed sentinel sites in Kuwait, troop medical clinics at Camp Arifjan and Camp Buehring, and two new sentinel sites, the naval hospital in Sigonella, Italy, and the branch medical clinic in Bahrain, were fully operational during the 2005–2006 influenza season. All four sentinel sites actively conducted influenza surveillance and added rapid diagnostic influenza testing to their laboratory capacity. More than 200 medical and laboratory personnel received GEIS influenza surveillance program training at these four sentinel sites.

The GEIS-supported Global Influenza Surveillance Program was strengthened by the addition of new sentinel sites in areas of strategic importance. Regional surveillance partnerships were also bolstered, which fortifies the GEIS pillars of cooperation and capacity building. The project brought together Navy medical, operational, and research units; Army medical and operational units; and the AFIOH to work jointly to improve regional surveillance activities. At the local level, command, medical, and laboratory staff received surveillance education and training, which improved support of surveillance efforts as an integral part of force health protection and public health infrastructure.

## **Brooke Army Medical Center**

The GEIS center of excellence for leptospirosis at Brooke Army Medical Center (BAMC) at Fort Sam Houston (Texas) has collaborated with the DoD overseas laboratories to develop diagnostic capabilities for leptospirosis to support deployed military troops. Servicemembers experience high rates of leptospirosis infection during operations in areas that are endemic for leptospirosis, which are frequently, but not exclusively, in the tropics.

Current diagnosis is not straightforward, which hinders identification and subsequent treatment. This work supports the GEIS pillars of surveillance, response, integration, and capacity building.

### **Surveillance**

BAMC, which includes the DoD reference laboratory for leptospirosis diagnosis, has provided expert interpretation of microscopic agglutination testing,

the gold standard for many febrile illness surveillance studies performed overseas. In addition, BAMC provided technical expertise in the diagnosis of leptospirosis, including currently evaluated PCR molecular probes and culture techniques. This support has resulted in numerous cultures obtained from Egypt and Thailand (using specimens provided by NAMRU-3 and AFRIMS, respectively) that have been used to characterize the serovars infecting people in different regions of the world that had not been characterized previously.

PCR technology in Egypt has greatly enhanced the epidemiological work underway at NAMRU-3. The leptospire species identified in Egypt from the multisite febrile illness surveys at NAMRU-3 include *Leptospira interrogans icterohaemorrhagiae*, *L. interrogans bataviae*, *L. interrogans grippotyphosa* (strain Andaman), *L. interrogans pomona*, and *L. interrogans pyrogenes*.

The epidemiological study from AFRIMS in Thailand revealed that out of 107 patients with suspected leptospirosis evaluated at a provincial hospital, 69 (65 %) were confirmed positive (titer > 1:800) by microscopic agglutination testing; 77 % ( $n = 53$ ) of cases occurred during the rainy season (June–November). Sera reacted predominantly with the Bratislava, Autumnalis, and Icterohaemorrhagiae serovars. The screening *Leptospira* Dip-S-Ticks had poor sensitivity (32 %) but 100 % specificity compared with *Leptospira* IgM ELISA. *Leptospirosis* was found to be a frequently confirmed cause of morbidity in some provinces of Thailand in those suspected of having the illness.

## Response

The BAMC surveillance with NAMRU-3 has enabled the development of treatment strategies in Egypt to ensure that leptospirosis is included in the differential diagnosis and that appropriate diagnostic tests are being performed. Therapy will also now include leptospirosis in endemic regions with the right clinical picture. Work in Egypt has also shown co-infections involving leptospirosis and brucellosis, *Rickettsia*, and typhoid fever; these findings will have a strong impact on future diagnostic and treatment strategies in this region.

## Integration

Many of the basic diagnostic platforms being evaluated at BAMC have allowed communication with the DoD overseas laboratories to strengthen diagnostic strategies in the field, including microscopic agglutination and molecular testing. The development of probes that can identify species of leptospirosis will enable a more rapid epidemiological characterization of febrile illness studies. The continued collection of leptospire isolates from around the world will enable GEIS and BAMC to create a repository of pathogens for future transition from epidemiologically based strategies to patient-based strategies that can be implemented at the time of diagnosis.

## Capacity Building

Several techniques developed at BAMC have enabled the center to assist the overseas laboratories in streamlining the evaluation of leptospirosis in local regions. For example, leptospirosis was cultured in humans and animals in Egypt by employing techniques and recommendations provided in previous work with animals and humans at BAMC. Continued improvement of the infrastructure at BAMC, especially molecular equipment including pulse-field gel electrophoresis, will enable better characterization of isolates through collaboration with the CDC to enhance the current knowledge of leptospirosis, thus further refining the work overseas. A deeper collaboration is also being developed with the CDC to establish a combined repository and fingerprint database for *Leptospira* species. This will develop into a powerful tool that will merge the leptospirosis detection capabilities of the foremost civilian laboratory interested in leptospirosis with the DoD surveillance and response network.

Through technical support from BAMC and GEIS on PCR methods for the detection of leptospires, NMRC in Peru has been able to implement a PCR-based surveillance tool for leptospirosis. This new technology will be part of an upcoming febrile illness study throughout Peru.

MTFs track medical records in real time using Clinical Information Systems (CIS) from CliniComp International (San Diego, CA). BAMC Infectious Disease Service personnel utilized the GEIS congressional supplemental funding for pandemic and avian influenza to develop a surveillance system that utilized software to survey the CIS patient records database every 5–10 minutes for influenza-like illness and other selected respiratory disease variables. This software had been used for a nosocomial febrile illness study at the Walter Reed Army Medical Center to identify patients eligible for enrollment in the study within minutes of developing a fever. The program was then adapted to query all active inpatients for fever and respiratory symptoms on admission. Patients meeting a case definition

were then screened and tested for respiratory pathogens by collecting nasal washes and submitting samples to the AFIOH, where specimens were evaluated according to protocol. This surveillance system has the potential for deployment at any MTF that uses the CIS and has personnel available to screen patients and collect clinical samples. Currently, all Army regional medical centers employ CIS. Although the rapid identification, screening, and gathering of clinical data in the most severe cases of influenza are of great public health interest, several additional projects could be pursued using the proposed surveillance system. For example, identified patients could be enrolled into research protocols to study the host response to influenza or to identify molecular markers for predicting severity of disease.

## *18th Medical Command*

### **Mosquito-, Rodent-, and Tick-borne Disease Surveillance**

Vector-borne diseases, including malaria, Japanese encephalitis, scrub typhus, leptospirosis, ehrlichiosis, and hantavirus pulmonary syndrome, are a health threat to the United States Forces Korea (USFK). Data from vector and disease surveillance provide the basis for maintaining readiness, a key issue for USFK personnel deployed to the Republic of Korea (ROK) and for a healthy fighting force throughout the DoD. For example, although malaria was eradicated from the Korean peninsula in the late 1970s, it reemerged in 1993, necessitating ongoing surveillance that has identified cases in USFK. Additionally, although no US cases of Japanese encephalitis have been reported in the ROK over the past two decades, isolations of Japanese encephalitis virus and a high percentage of serologically positive pigs demonstrate that the virus is still present, that transmission within the animal population occurs, and that human cases could occur.

Headquartered in Seoul, the 18th Medical Command (MEDCOM), Force Health Protection, conducts historical analysis of malaria and other endemic, reemerging, and newly described human pathogens throughout Korea. In addition, 18th MEDCOM performs routine mosquito surveillance in Korea to identify 1) geographical and spatial

population trends, 2) location of mosquitoes harboring disease threats to determine areas of potential transmission, and 3) infection rates of malaria and Japanese encephalitis in mosquitoes. Adult mosquito surveillance is conducted annually from 15 May through 15 October and provides a basis for initiating adult mosquito control. Areas surveyed are those where soldiers are at greater risk and where generally larger biting populations of mosquitoes are experienced. These GEIS-sponsored studies provided invaluable information for epidemiological investigations and disease control programs and gave the 18th MEDCOM, and ultimately PACOM, specific information to recommend vector control for high-risk areas. Accurately targeting of high-risk areas reduces disease incidence rates and provides cost savings to PACOM.

Mountains comprise approximately 70 % of Korea's landscape. Wetland rice farming is the predominant agriculture among the scattered fertile valleys and is largely responsible for sizeable mosquito populations. The mountainous topography and somewhat isolated river valleys create the potential for focal transmission of malaria, arboviruses, and other tick-, mite-, and rodent-borne diseases. For example, an unidentified Hantavirus has been associated with the Imjin River system and could cause human disease. In Korea, human populations and agriculture are centered around villages, towns, and cities within the valleys and river systems, unlike



## *EUCOM Influenza Surveillance Expands*

With the FY06 supplemental funding for pandemic and avian influenza, GEIS supported Landstuhl Regional Medical Center in Germany to expand and integrate laboratory and epidemiological work of the DoD Global Influenza Surveillance Program in Europe. This expansion is enabling Landstuhl to increase its testing workload to include the triservice clinics/hospitals throughout EUCOM. In addition, Landstuhl will renovate its laboratory to become the only US BSL-3 laboratory in the EUCOM area of responsibility.

The expanded laboratory capability will allow more specimens to be processed, isolation to be performed under BSL-3 conditions, and a larger geographic area to have timely laboratory services. This capacity will benefit influenza surveillance and would allow Landstuhl to support EUCOM in an intentional outbreak of infectious disease, such as anthrax or plague. Landstuhl is also a first stop in the air evacuation system for deployed forces. Most casualties transported from CENTCOM receive care at Landstuhl, so an infectious disease pathogen in EUCOM or CENTCOM will quickly be at Landstuhl with its full laboratory resources.

In previous years, Landstuhl received specimens from Germany and from a few facilities in CENTCOM in direct support of Operation Iraqi Freedom. Specimens from sentinel MTF sites in Europe have been routinely sent to AFIOH for processing. For the 2006–2007 influenza season and beyond, Landstuhl has expanded its testing capabilities through a FY06 effort coordinated by GEIS and AFIOH with Army, Navy, and Air Force leadership and with guidance from the EUCOM Surgeon. Sites are projected to include Belgium, Germany, Italy, Portugal, Spain, Turkey, and United Kingdom. CHPPMEUR has also established working relationships and training to support an expanded influenza surveillance mission. Should a novel influenza strain appear in US forces in EUCOM or CENTCOM, which includes Europe, Africa, and southwest Asia, this collaborative effort will enhance the ability and capacity of DoD to collect high quality specimens, identify the agent, quickly characterize an influenza outbreak, and determine the need for additional preventive measures, all of which will reduce morbidity and mortality.

During the 2005–2006 influenza season, Landstuhl tested nearly 800 specimens and expects to dramatically increase that number in the 2006–2007 season. Thanks to support from AFIOH, Landstuhl will have the capability to perform typing and subtyping of influenza specimens and will perform sequencing of the hemagglutinin genes in comparison with human vaccine component strains. Landstuhl has developed real-time PCR assays for influenza and RSV detection in conjunction with viral culture results and, during the last influenza season, developed and validated additional assays for adenovirus, parainfluenzaviruses, and enteroviruses that will be utilized during the upcoming season.



Actual and potential European locations of US forces under sentinel surveillance that will benefit from enhanced Landstuhl/CHPPMEUR collaboration with the DoD global influenza surveillance system during the FY06 influenza season and into FY07.



other regions in Asia where families reside on the land that they farm. Military bases are often associated with clustered civilian populations. This arrangement creates areas of dense populations, which can magnify the potential for focal transmission. Travel outside these areas of concentrated populations compromises containment of focal disease transmission within the country, possibly leading to further dissemination of malaria and other diseases throughout Korea. This puts civilian and military populations at risk of infectious diseases to which they would not be exposed in other areas of the world.

Long-term GEIS funding for mosquito-, rodent-, and tick-borne disease surveillance has enabled 18th MEDCOM to provide commanders and staff with the following:

- Analysis of vector-borne disease trends;
- Spatial and geographical high-risk areas based on historical, field, and epidemiological data;
- Review of military performance in disease mitigation strategies (e.g., lack of emphasis and implementation of personal protective measures);
- Identification of new and emerging diseases.

Through GEIS, 18th MEDCOM is conducting a vector-borne disease program that contains elements of historical analysis to identify trends of vector populations and disease, effects of vector and disease mitigation strategies on disease rates, and vector-borne disease surveillance. West Nile virus was recently introduced into the United States and spread across the North American continent. Concern about West Nile has prompted the Korea National Institute of Health to develop plans for the possible introduction of West Nile virus into Korea. Realizing that West Nile virus or other as yet unidentified emerging infectious agents may threaten in the future, GEIS has provided the foundation for the development and implementation of broad vector-borne disease surveillance in Korea that can cover many pathogenic agents.

### Surveillance for Chlamydia Among Female Soldiers Assigned to ROK

Chlamydia is the most frequently reported and prevalent sexually transmitted infection in the US civilian and military populations. Among regularly

screened females in the United States (civilian and military), the documented rates of chlamydia in 2006 ranged from 4% to 14%, with 4 million new cases annually. The significant health problems for females that are directly attributed to chlamydia infections include ectopic pregnancy, pelvic inflammatory disease, and chronic reproductive complications including infertility. For the United States, some estimates of the costs associated with the treatment of these complications exceed \$10 billion in the year 2000, with costs continuing to rise.

For the US military, the response in managing chlamydia has been mixed. Both the Navy and Marine Corps have a point-of-entry screening process for female recruits. However, neither the Army nor the Air Force has applied such a policy. Rather, each recommends that sexually active females younger than age 25 obtain a chlamydia screen within their first year of service. For the Army, several large-scale surveillance studies have analyzed both the prevalence of chlamydia in recruits and the potential benefits if such a screening process were to be implemented. The medical benefit and cost savings of screening programs are documented. By using the Korea project as a template, GEIS will create a surveillance model that may be implemented at other military in-processing centers for newly assigned military personnel.

The GEIS population-based prospective surveillance study at 18th MEDCOM was designed to determine the prevalence and risk factors for *Chlamydia trachomatis* infection among active duty female soldiers assigned to the Eighth US Army and subordinate commands in the ROK. US female soldiers deployed to Korea submitted a urine sample during the 1- to 7-day reception period at in-processing centers in Yongsan Garrison (Seoul) and Camp Casey (Dongducheon) from 1 July 2003 to 31 July 2005. Urine samples were analyzed for *C. trachomatis* at the 121st General Hospital (Seoul) or at Tripler Army Medical Center (Honolulu). Results were forwarded to the community health nurse at 18th MEDCOM and the regional emerging infectious disease consultant within 7–12 days for entry into the study database. Positive results were forwarded to the contagious disease surveillance specialist and the responsible community health nurse for management. Analysis of data assessed the prevalence of *C. trachomatis*

and identified decreases in the overall *C. trachomatis* infection rate among US female soldiers stationed in the ROK.

A query of female soldiers positive for *C. trachomatis* by age group demonstrated that the highest risk age population was 19–25 years (Figure 11). At age 26, the percent of infections was 6.3 % and decreased to a low of 0.5 % for those aged 40 years (mean 4.0 %). Detection of asymptomatic *C. trachomatis* infections in females and prompt treatment are significant measures that will prevent complications in the infected individual and limit the spread of this infection. Ascertaining the exact prevalence and contributing

risk factors for asymptomatic infections will enable more focused and effective countermeasures to protect the health of the force.

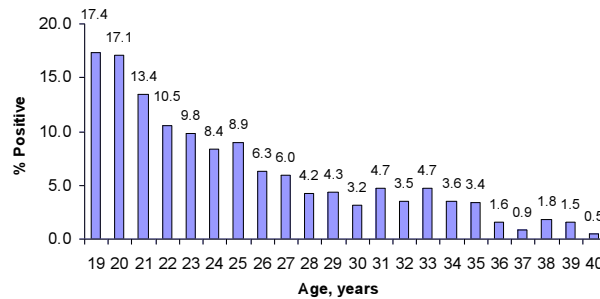


Figure 11. Positive *C. trachomatis* infection in female Eighth US Army soldiers by age; overall percent positive for *C. trachomatis* was 8.1 %.

## Office of the Assistant Secretary of Defense for Health Affairs

Real-time disease outbreak detection and the ability to forecast outbreaks before an index case presents for medical care are desirable end states in a world concerned about emerging infectious diseases, whether of natural or deliberate origin. Detection and forecasting require different data and analytical methods than traditional approaches to public health. Few offices in the MHS focus on independently developing new techniques and/or evaluating those arising in academia or industry for possible adoption by the MHS. Consequently, GEIS supported the Office of the Assistant Secretary of Defense for Health Affairs to refine disease surveillance techniques to maximize the ability of the military to detect, identify, validate, characterize, and/or predict disease outbreaks at the earliest opportunity.

Such epidemiologic surveillance techniques will be especially useful because they generally apply to

many kinds of disease outbreaks or clusters, although initial work will focus on improving the ability to identify infectious disease outbreaks, such as SARS and avian influenza or any caused by biowarfare agents. The solutions must address the disparate needs found in the garrison and deployed settings. Improved surveillance will maximize the time available to prevent or mitigate the outbreak, which in turn will minimize the impact on the DoD beneficiary population and military operations/readiness.

Staff and a network of methods developers have been established. A detailed, prioritized work plan is in development to identify and evaluate potential data sources, develop best-fit analytical detection algorithms, and integrate disease modeling techniques.

## Uniformed Services University of the Health Sciences

GEIS provides tropical medicine field training for DoD and US government personnel through the Uniformed Services University of the Health Sciences (USUHS). In support of the GEIS pillar of capacity building, the objective is to develop and monitor tropical medicine and surveillance curricula for students, residents, fellows, and others training in overseas locations. The project facili-

tated data sharing between USUHS and the DoD overseas laboratories and provided opportunities for consultation and assistance by the students to the staff at the laboratories. Students of various disciplines were given practical experience in tropical medicine research within the overseas laboratories and military field units.

In FY06, 35 individuals completed the USUHS training: 14 medical students, eight participants in military tropical medicine course field missions, three masters in tropical medicine and hygiene students, three residents, three infectious disease fellows, and three MPH/PhD/DrPH candidates. Students participated in research projects with AFRIMS, USAMRU-K, NAMRU-3, and NMRC in Honduras. The relationship of GEIS with JTF-Bravo stems from the GEIS surveillance work in Central America through USACHPPM-West that requires regular interaction with JTF-Bravo.

Projects included assisting the conduct of enteric disease studies in Turkey (through NAMRU-3 in Cairo), nutritional surveys in Honduras (through

NMRC in Lima), malaria research on the Burmese border (through AFRIMS in Bangkok), and brucellosis research in northern Queensland, Australia. Additionally, two students were funded for 1-month tropical medicine educational experiences in Sri Lanka. One physician participated in a Pacific Air Forces mission to Fiji where his skills and knowledge of the local language were invaluable.

This GEIS training has furthered the corporate knowledge of the military health professionals by providing direct hands-on experience in conducting tropical medicine field research with expert faculty. As knowledge of the program grows, the training opportunities and collaborations around the world are expected to increase and benefit the US military.

### *Center for Disaster and Humanitarian Assistance Medicine*

The Center for Disaster and Humanitarian Assistance Medicine (CDHAM) is a USUHS organization with a mission to be the focal point for medical aspects of disaster relief and humanitarian assistance worldwide. In contrast to other humanitarian relief groups that focus on disaster management, CDHAM specializes in medicine and health care.

For the last 2 years GEIS has had a collaborative relationship with CDHAM to maintain and build partnerships within the DoD, the US government, the international community, and other organizations active in disease surveillance and rapid response. GEIS funds CDHAM to assist the five geographic combatant commands (COCOMs) in developing emerging infectious disease plans for humanitarian emergencies such as earthquakes, tsunamis, epidemics and war.

In FY06, GEIS funded CDHAM to support the COCOMs in concept development, planning, and

execution of education and training programs for influenza surveillance and response in each COCOM area of responsibility. Additionally, CDHAM provided technical assistance by reviewing the strategic setting of the COCOMs, analyzing operational and contingency plans, and evaluating those plans against the National Strategy for Pandemic Influenza. In particular, CDHAM assisted the PACOM, NORTHCOM, and SOUTHCOM in identifying areas that would benefit from additional interagency interaction, workshops, and training.

CDHAM will continue to focus on building capacity within each COCOM region through information sharing, technology, laboratory enhancement, and training and education. These efforts will augment the ability of GEIS to gain and expand knowledge on regionally specific threats related to influenza and potentially other emerging infectious diseases.

# DoD Overseas Laboratories

## Naval Medical Research Unit No. 2

### Jakarta, Indonesia

GEIS projects at Naval Medical Research Unit No. 2 (NAMRU-2) have been on the forefront of the characterization and mitigation of regional infectious disease threats and have assisted developing countries to build effective outbreak surveillance, investigative, and diagnostic infrastructures. NAMRU-2 has fostered an extensive network of collaborative relationships throughout the region and with countries vulnerable to new or reemerging pathogens, such as influenza A H5N1 virus (highly pathogenic avian influenza) and with countries facing public health emergencies, such as a tsunami and an earthquake.

The importance of GEIS surveillance at NAMRU-2 was recently supported by a November 2006 article in the *Proceedings of the National Academy of Sciences* in which the confounding and troubling behavior of the H5N1 virus found in poultry throughout China is detailed. The authors state that despite the achievements of the Chinese surveillance network, “there remains a lack of information in the broader region, and it is critical that similar surveillance programs begin in other areas, including Indonesia, Vietnam, Thailand, and India.”<sup>1</sup> GEIS is uniquely positioned to fill this need with its established and growing surveillance network, including NAMRU-2.

Highly pathogenic avian influenza highlights the issues of regional disease spread and the crucial role of GEIS at NAMRU-2 in conducting disease surveillance, case/outbreak investigation, and diagnostic support. NAMRU-2 either identified or shared in the confirmation of all human cases of H5N1 infection in Indonesia (Figure 12; 72 as of 16 October 2006), and the NAMRU-2 laboratory is recognized as one of two human H5N1 reference laboratories by the Indonesian Ministry of Health. On average, NAMRU-2 tests specimens from ~ 100 suspected human H5N1 cases each month. Positive

blood or respiratory samples are shipped to the CDC for verification and genetic sequencing and for assay and vaccine development. Data are shared with the Indonesian Ministry of Health and WHO.

During FY06, GEIS-supported avian and pandemic influenza surveillance at NAMRU-2 was further developed into a comprehensive program encompassing animals and humans. These efforts include surveillance of influenza viruses in migratory birds on Java, a passive surveillance network to detect influenza viruses in humans with influenza-like illness or diarrhea with acute respiratory symptoms in Indonesia, and development of new human surveillance and diagnostic capabilities in Lao PDR and Cambodia. This network tests more than 500 human specimens per month and collected 695 serum samples, 697 throat swab samples, and 698 cloacal swab samples from 64 species of domestic, resident wild, and migratory birds. Human specimens positive for H5N1 and other influenza viruses were shipped immediately to the CDC.

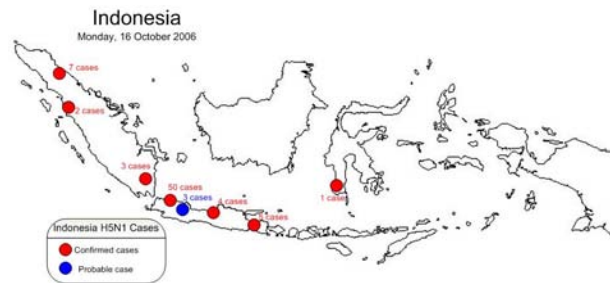


Figure 12. Locations of confirmed and probable human H5N1 cases in Indonesia.

With GEIS support, NAMRU-2 upgraded equipment to conduct onsite genetic sequencing to detect potential pandemic mutations and increase the volume of specimens that can be tested with real-time RT-PCR. In addition, a multiplex assay system called Luminex xMAP is being deployed in

<sup>1</sup> Smith GJ, Fan XH, Wang J, et al. Emergence and predominance of an H5N1 influenza variant in China. *Proc Natl Acad Sci USA* 2006;103(45):16936–41.



Cambodia and Lao PDR to test multiple specimens simultaneously for multiple respiratory pathogens, including influenza A H5N1 (this assay system will support Ministry of Health case and outbreak investigations and NAMRU-2 studies in FY07).

NAMRU-2 provided direct medical support in response to the magnitude 6.3 earthquake near Yogyakarta, Java, on 27 May 2006 that resulted in more than 5,000 deaths. In addition to supporting civilian operations by providing medical care to the injured, NAMRU-2 personnel supported 3rd Marine Expeditionary Brigade by assisting in identifying a suitable site for the brigade's medical team, providing liaison with local hospitals, clinics, and communities to establish patient sources, and providing translators. These critical actions supported both civilian and military operations.

Through GEIS, NAMRU-2 supplied field and/or diagnostic support for infectious disease outbreaks in three Southeast Asian countries: an acute jaundice syndrome (hepatitis A) outbreak in Lao PDR, dengue hemorrhagic fever outbreaks and gastroenteritis outbreaks in Indonesia, and acute upper respiratory and diarrhea outbreaks in Cambodia.

Civilian and military operations continue to benefit from GEIS support through ongoing NAMRU-2 surveillance for significant diseases in the region, including malaria and diarrheal diseases. Malaria and diarrheal diseases widely affect civilian populations and are leading infectious disease threats to the US military. In Indonesia, a prevalence-anti-malarial genetic marker study on Sumba has laid initial groundwork for the development of future studies of antimalarial drugs. Furthermore, NAMRU-2 conducted a bionomics study to investigate the primary vectors that transmit malaria to document the spatial and temporal species-specific vector distribution and bionomics over a year and to identify correlates with disease risk in endemic foci in West Java, Indonesia. A NAMRU-2 study of diarrhea in Indonesia found that rotaviruses contribute a substantial burden of disease. This study enhances situational awareness for PACOM commanders and will enable the ministry of health to conduct preliminary analyses for the implementation of newly tested rotavirus vaccines. Final logistical preparations have been completed toward

the implementation of an acute febrile illness surveillance study in Cambodia, with the first enrollment of patients expected in December 2006.

In collaboration with NMRCDC, the GEIS Headquarters, and the Johns Hopkins University/Applied Physics Laboratory (JHU/APL; Baltimore, MD), NAMRU-2 evaluated the Early Warning Outbreak Recognition System (EWORS) in Lao PDR (Figure 13). EWORS is an innovative syndromic surveillance system for early detection of disease outbreaks that was developed and successfully implemented in Indonesia using GEIS funding at NAMRU-2. This collaboration will assist in further development of EWORS, in particular as a tool to improve response to pandemic influenza.



Figure 13. Members of EWORS Working Group visiting Lao Ministry of Health to collect data for adapting EWORS modeling for pandemic influenza.

GEIS also supported several training projects at NAMRU-2 to build regional capacity for response to infectious disease threats. NAMRU-2 personnel provided training in influenza A H5N1 diagnostic assays to the Indonesian Ministry of Health and AFRIMS in Bangkok. Scientists from the Indonesian Ecology and Health Status Research and Development Center and the Indonesian National Institute of Health Research and Development participated in didactic and laboratory training at the University of Iowa Center for Emerging Infectious Diseases. Further training in microbiology, biostatistics, and malaria microscopy was conducted with the Indonesian Ministry of Health and the University of Indonesia. In addition, microbiology and surveillance training is provided to laboratory technicians from the Cambodian Ministry of Defense.

In continued support of the GEIS pillars of cooperation, capacity building, and integration, NAMRU-

2 shared its results, resources, and expertise with collaborators from regional ministries of health and with other branches of the US military. Conferences and publications as well as close information sharing with the GEIS Headquarters mean that data are shared with the scientific community and the DoD.

Through GEIS Headquarters staff and funding support, NAMRU-2 made significant contributions to understanding disease threats in the region. This

support facilitated the rapid identification of human influenza A H5N1 infection and the rapid delivery of specimens with virus to the CDC, which means potential improvement of diagnostic assays and vaccine development. Innovative studies have led to the new understanding of emerging and reemerging pathogens, their vectors, and their environment. NAMRU-2 continues to contribute to the regional development of diagnostic capabilities to prepare collaborators to respond to infectious disease threats.

### Naval Medical Research Unit No. 3 *Cairo, Egypt*

GEIS work at Naval Medical Research Unit No. 3 (NAMRU-3) was directed primarily toward nine projects that were continued from FY05. Three programs were started in FY06, the most significant of which was the development of a rotavirus surveillance network in the eastern Mediterranean region. The other new programs were surveillance for antimicrobial resistance in nosocomial infections and identification of reservoir hosts for *Leishmania* species in the Volta Region of Ghana.

Surveillance for avian influenza and other respiratory viruses in the Middle East, Africa, and Eastern Europe constituted the most important GEIS-supported effort at NAMRU-3 in FY06. Like other GEIS-supported overseas research laboratories, NAMRU-3 received supplemental funding for pandemic and avian influenza surveillance and response activities in FY06 aimed at increasing capacity, capability, and geographic coverage. With the continuing spread of highly pathogenic avian influenza and the threat of pandemic influenza, regional partners must sustain systems that allow robust early warning. As a WHO Regional Influenza Reference Laboratory, NAMRU-3 is on the frontline of coordinating collection and shipment of specimens, performing diagnostic testing, and reporting results to international organizations. Accordingly, in FY06, NAMRU-3 processed more than 3,200 animal and human specimens from 12 countries to evaluate avian influenza infection. Furthermore, to ensure that seasonal influenza strains circulating in the region were considered in the decision for the annual seasonal vaccine,

NAMRU-3 collected and processed an additional 3,000 human specimens from individuals with influenza-like illness, of which a subset of isolates was forwarded to the CDC in Atlanta for further characterization.

As part of the surveillance for hemorrhagic fever viruses and arboviruses, NAMRU-3 collected more than 1,500 specimens in FY06. Test results from these specimens resulted in several outbreak responses to control both dengue and yellow fever. In addition, a recent death of a local civilian in Kabul, Afghanistan, was attributed to Crimean-Congo hemorrhagic fever after a specimen from the victim was processed and analyzed at NAMRU-3. This case resulted in immediate feedback to the DoD and Department of State. It also strengthened the partnerships formed among NAMRU-3 and the Afghan Ministry of Health, Food and Agriculture Organization of the United Nations, WHO, CDC, and Combined Forces Command.

During FY06, laboratory-based surveillance continued in Egypt for acute febrile illnesses, which can be difficult to diagnose clinically because symptoms overlap those of many conditions. NAMRU-3 demonstrated the importance of distinguishing brucellosis, leptospirosis, and rickettsiosis by developing PCR tests for specific agents. Capacity building was guided toward training for bacterial culture and serological testing at three infectious disease hospitals in Egypt. A notable result was obtaining > 65 *Leptospira* isolates from patients. This is the first report of confirmed

human leptospiral cultures in Egypt. Acute infection, with at least two zoonotic organisms, was also confirmed in 24 (1.6%) acute febrile illness patients by culture, PCR, or a four-fold rise in antibody titers. Many patients (n = 22) were confirmed to be simultaneously infected with three pathogens: *Leptospira*, *Rickettsia typhi*, and *Brucella* or *Salmonella enterica* subsp. *typhi*.

A new nosocomial surveillance system was implemented at several ministries of health and university hospitals throughout Egypt. At more than 18 general hospitals, NAMRU-3 trained 75 staff members in surveillance and laboratory procedures. Rates for surgical, bloodstream, and urinary tract infections ranged from 4.7 to 60% at different hospitals. A high proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum beta-lactamase (ESBL) strains were detected among *S. aureus* (65%) and *Klebsiella pneumoniae* (96%) isolates, respectively. The high proportion of MRSA and ESBL isolates suggests an emerging problem in Egypt, and further antimicrobial susceptibility studies will be conducted to monitor these trends throughout the Middle East. In addition, these high infection rates demonstrate the need for continuous infection surveillance in the healthcare system in Egypt.

Regional activities focused on continued strengthening of laboratory capacity and the implementation of a regional network for bacterial meningitis surveillance efforts across the Middle East. During 2006, Morocco and Libya joined Yemen, Syria, Pakistan, and Sudan in the surveillance network for bacterial meningitis. More than 100 personnel have been trained at 32 hospitals in six countries in effective laboratory practices and surveillance activities. More than 6,000 cases have been enrolled, and laboratory supplies have been distributed accordingly. The current data indicate that *Neisseria meningitidis* was the most common etiology identified that causes bacterial meningitis in Sudan. In contrast, *Streptococcus pneumoniae* was the leading cause of bacterial meningitis in confirmed cases in Pakistan, Syria, and Yemen. For the first time, this ongoing laboratory-based surveillance is contributing to the understanding of bacterial meningitis epidemiology across the Middle East and is guiding meningitis vaccination strategies.

A considerable effort was directed toward the advanced characterization of *S. enterica* subsp. *typhi* (typhoid fever), *S. pneumoniae*, and *Brucella melitensis* isolates. Pulsed-field gel electrophoresis of *S. enterica* subsp. *typhi* isolates demonstrated high similarity rates among collections. This technique could facilitate early detection and control of typhoid fever outbreaks as well as assist in tracking multidrug resistance across the region. Based on multilocus sequence typing analysis for *S. pneumoniae*, NAMRU-3 reported 14 new sequence types and two new housekeeping gene alleles for Egypt. By using two new multilocus variable number repeat analysis procedures, NAMRU-3 characterized *B. melitensis* isolates from Egypt and Qatar. Both procedures discriminated all isolates into distinct genotypes. Isolates from Egypt and Qatar clustered largely into separate groups; however, no clustering was observed by specific collection site. Both procedures are highly discriminatory and can be used to evaluate phylogenetic relationships in *B. melitensis*.

In early 2006, GEIS supported NAMRU-3 to serve as the Eastern Mediterranean Rotavirus Surveillance Network reference laboratory starting with five countries: Egypt, Iran, Morocco, Pakistan, and Tunisia. Libya was added later in the year. A training workshop was held in Cairo in December 2006, during which Jordan, Sudan, Syria, and Yemen were enrolled.

Supporting the GEIS pillar of response, NAMRU-3 investigated 25 disease outbreaks in FY06 that encompassed eight conditions in 11 countries. In Iraq and Afghanistan, a NAMRU-3 detachment investigated infectious disease outbreaks in support of Operation Iraqi Freedom and Operation Enduring Freedom to identify avian influenza, *Coxiella burnetii* (Q fever), malaria, Crimean-Congo hemorrhagic fever, diarrheal diseases, and *Leishmania*.

A notable response effort was the NAMRU-3 investigation of an outbreak of leishmaniasis in the Ho District, Volta Region, of Ghana, which increased the host nation capacity to isolate and detect the *Leishmania* parasite. Preliminary data suggest that two *Leishmania* species, *L. major* and an as yet unconfirmed species, may be involved. An important consequence of this study is an increased

ability of Ghana to diagnose and respond to future outbreaks of disease, and the ability of NAMRU-3 to present collaborative reports to the Ministry of Health and the Ghana Health Services to make recommendations guiding the prevention of leishmaniasis, thus affecting the overall health of the country. Establishing this trust and rapport with the health services in Ghana, which supports the GEIS pillars of cooperation and capacity building, is crucial for future epidemiological studies in Ghana and West Africa.

Further fulfilling the GEIS pillars of cooperation and capacity building, and in its responsibility as a reference laboratory, NAMRU-3 extended its experience and knowledge throughout the region. Training workshops on epidemiology and laboratory procedures, which were conducted on- and off-

site, reached more than 150 scientists from 20 countries. Topics included specimen collection, diagnostics, shipping, molecular procedures, and biosafety for many bacterial and viral agents. These activities have increased the capacity of regional partners in the CENTCOM and EUCOM areas of responsibility to effectively isolate, identify, and characterize pathogens of global importance.

NAMRU-3 GEIS outbreak responses provided host countries with infectious disease information and CENTCOM and EUCOM commanders with evidence to increase situational awareness regarding disease threats in their areas of operation. NAMRU-3 also trained host nationals to develop a rapid response capability for an array of microbial threats to limit the severity of future outbreaks and reduce disease threats to US forces in the region.

## Naval Medical Research Center Detachment

### *Lima, Peru*

The Naval Medical Research Center Detachment (NMRCD) continues to be the sole overseas medical research unit for the DoD in the Western Hemisphere. With this unique position, NMRCD serves an essential role in the global surveillance and response network for emerging infectious diseases that comprises a key component of the GEIS mission. The following are integral to the GEIS work through NMRCD in South America, particularly in support of SOUTHCOM: outbreak response preparation; detection, investigation, and identification of microbial agents; and communicable disease control and prevention.

### Alignments

During FY06, NMRCD made concerted efforts to align the GEIS work with the missions and goals of SOUTHCOM. In collaboration with SOUTHCOM, NMRCD determined priority countries for infectious disease surveillance and research. Because Colombia is the highest priority for SOUTHCOM, NMRCD expanded efforts in the following areas:

- Electronic surveillance for infectious disease in the Colombian military has been approved and will commence in FY07;

- Surveillance for HIV and other sexually transmitted infections will be initiated in several sites;
- Influenza surveillance will be expanded;
- Monitoring of several parasitic infections, particularly malaria and leishmaniasis, will begin.

Alerta DISAMAR, the electronic disease surveillance system pioneered in the Peruvian military, has been approved by SOUTHCOM to expand on a regional scale to include five additional countries: Ecuador, Colombia, Bolivia, Paraguay, and Uruguay. The effort to initiate these sites has begun and will continue through FY07.

The GEIS program at NMRCD also developed collaborations with other military and nonmilitary organizations. As with SOUTHCOM, NMRCD worked with US Army South, in support of Operation New Horizons in Peru, and with USACHPPM-West. In the nonmilitary setting, NMRCD coordinated with the CDC Global Disease Detection laboratory in Guatemala City, particularly in the area of training for outbreak detection and response. Two NMRCD staff members went to Guatemala in November 2006 to participate as



faculty in an avian influenza outbreak response conference, which is offered to all countries in Central America.

Collaborations with the Pan American Health Organization and several ministries of health in the training of outbreak management continued. An influenza pandemic scenario was prepared and presented at the regional USAID pandemic influenza preparedness meeting, held in May 2006 in Lima. In addition, a CDC staff scientist was hired who will augment the NMRCDC capability in influenza outbreak detection and response, influenza surveillance, and hemorrhagic fever expertise. Continued collaboration with scientists and epidemiologists from the Peruvian Ministry of Health, Navy, and Army has strengthened the network for effective response to disease outbreaks.

To help standardize surveillance throughout the GEIS network, NMRCDC partnered with the GEIS Headquarters, JHU/APL, and NAMRU-2 to optimize and implement EWORS. Throughout the year, NMRCDC developed and refined EWORS in Peru and ultimately participated in a conference in Lao PDR to help NAMRU-2 enhance EWORS there. The knowledge and real-world experience from another developing country offered by NMRCDC led to improvements for this next iteration of EWORS that will improve pandemic influenza preparedness. NMRCDC also developed the analytical software and the mathematical algorithms for EWORS and optimized the performance of the software in Spanish. At the 2006 International Conference on Emerging Infectious Diseases in Atlanta, NMRCDC scientists presented four abstracts based on EWORS.

Disease outbreaks from dangerous pathogens, either naturally or intentionally occurring, are an ongoing concern for GEIS. Through GEIS connections with Peruvian Ministry of Health, NMRCDC identified several naturally occurring cases of disease caused by various agents. This project, which was leveraged through funding from the biodefense group of the Department of Homeland Security and Biological Defense Research Directorate at NMRC, collected specimens of from cases of cutaneous anthrax, bubonic plague, brucellosis, Venezuelan equine encephalomyelitis, and Hantavirus. These specimens were characterized locally and sent to the United States for further advanced testing. This work directly supports the GEIS pillar of surveillance.

## Overview of Projects

The palette of GEIS projects at NMRCDC reflects a coordinated effort to provide comprehensive infectious disease surveillance for South America. Internal symposia continue to be organized to discuss ongoing projects, budgets, alternate funding sources, and future directions of the program with relation to the goals of GEIS and the overall mission of the laboratory. These meetings foster cooperation among the departments and update the officer-in-charge about ongoing projects.

The largest expansion in GEIS infectious disease surveillance at NMRCDC has been in actions connected with influenza. Additional funding in FY06 allowed vital growth in laboratory capability, and the number of specimens collected and sentinel sites increased accordingly, directly supporting the GEIS pillar of capacity building. In the past, NMRCDC has relied on AFIOH for all viral isolation and identification; specimens were stored and shipped in batches. Thus, results often were unavailable for several weeks to months. During FY06, in-house capability to detect influenza improved, including establishment of viable cell culture, real-time PCR, and gene sequencing, which are now routinely performed at a dedicated virology section laboratory in Lima. This local capacity now allows results to be rapidly returned to providers, keeping collaborators engaged and patients satisfied with the results. NMRCDC continues to send isolates to AFIOH, which makes isolates available to the CDC respiratory pathogen program.

Surveillance for febrile illness pathogens expanded, leveraging the increased number of sites for respiratory disease surveillance. NMRCDC continues to isolate novel viruses through this program; for example, dengue 3 and dengue 1 were isolated this year. This finding is important because the presence of multiple serotypes of dengue circulating in a geographic area suggests the risk of dengue hemorrhagic fever. In addition, NMRCDC detected a three-fold increase in Venezuelan equine encephalomyelitis cases and initiated more intensive study. Other viruses such as Ilhéus, Oropouche, and Caraparu were also isolated, and a South American strain of Eastern equine encephalitis virus has been found in Iquitos, prompting more extensive investigation. In FY06, the febrile surveillance study collected more than 3,000 specimens from 11 sites in Ecuador, Peru,

and Bolivia, with an isolation rate of 26 %. The number of sites will increase with further leveraging of the respiratory surveillance program.

Enteric pathogen resistance patterns continue to be the focus of the bacteriology program at NMRCDC, which has also branched into surveillance for brucellosis and sexually transmitted infections. This year, the trend of increasing resistance among *Campylobacter* species to fluoroquinolones continued, matching trends found in other regions of the world. Interestingly, the resistance patterns of *Shigella* and *Salmonella* isolates to azithromycin have been decreasing since 2000, probably reflecting change in treatment to erythromycin. GEIS-NMRCDC surveillance for gastroenteritis syndromes among Peruvian military populations, and among travelers and US embassy personnel, continues. In terms of sexually transmitted infections, molecular technology is being used to track fluoroquinolone resistance among *Neisseria gonorrhea* and *Treponema pallidum*. Also through GEIS, NMRCDC has developed novel methods to isolate *Brucella* more rapidly.

The parasitology program continues to expand surveillance of antimalarial resistance using real-time molecular techniques. In addition, in response to a request by SOUTHCOM, GEIS staff began to study rates of *Leishmania* in Colombia. SOUTHCOM assists Colombian forces in interdiction efforts in the war on narcotics, which involves troops working in areas with increased exposure to the *Leishmania* parasite. This investigation supports the GEIS pillar of cooperation, which benefits both the host nation and the US military. NMRCDC has also been instrumental in responding to several outbreaks of diarrheal disease caused by *Cyclospora cayentanensis*. A multiplex PCR test is being evaluated that will be able to detect in real time the presence of *Cyclospora*, *Cryptosporidium*, and *Giardia*. If successful, this technique would allow faster and more reliable identification of pathogens in a sample.

Among the most vital of NMRCDC capacities is the continued ability to conduct comprehensive outbreak investigations. GEIS staff continue to provide formal and informal advice and laboratory support and deployed full epidemiological teams to respond to requests for assistance. NMRCDC continues to partner with the Peruvian Ministry of

Health to respond to outbreaks of disease when asked. During FY06, NMRCDC responded to outbreaks of dengue in Tumbes and Iquitos, several outbreaks of diarrhea among Peruvian military forces, one leptospirosis outbreak in Lima, a yellow fever outbreak in the remote Amazon jungle, and a plague and anthrax outbreak in northern Peru. Outside of Peru, epidemiologic and laboratory support was provided to Bolivia for a Hantavirus epidemic.

An important GEIS response at NMRCDC in FY06 involved the investigation of a large outbreak of diarrhea among SOUTHCOM forces in Peru for 2 months during Operation New Horizons. This exercise took place in Chiclayo, on the northern coast of Peru, and led to many cases of diarrhea. NMRCDC responded by deploying laboratory technicians and two physicians to identify the source of the outbreak. The command element was pleased with the support and has requested assistance with a similar exercise to be held next year in Guatemala and Panama. Diarrheal diseases are significant to GEIS and the DoD because they are leading causes of disease nonbattle injury for military forces and can dramatically impair troop readiness during exercises and on the battlefield.

Pack-out kits for outbreak response efforts have been standardized, and several are ready for immediate transport. A standard operating procedure has been developed for outbreak investigation response so that each department can efficiently respond to requests for assistance while keeping the GEIS Headquarters informed. Scientists, clinicians, epidemiologists, veterinarians, and entomologists continue to be cross-trained so that multiple roles can be filled when the need arises. A formal outbreak training course for NMRCDC personnel was held in October 2005 and was well received by senior laboratory technicians and investigators.

Formal classroom training in outbreak investigation, a major GEIS function at NMRCDC, was presented to public health officials in Peru, Argentina, Chile, and Suriname. NMRCDC scientists and senior laboratory technicians are often among the teachers of these courses. In addition to building the public health capacity of these countries, a GEIS pillar, these courses often serve as a springboard for future collaborations with scientific departments. For example, ongoing febrile surveillance in Paraguay

and Bolivia was built in this manner after NMRCDC personnel taught courses in these countries. Collaborations continue with the Pan American Health Organization and regional ministries of health to share costs for these courses, for which both organizations provide instructors.

After developing a similar course for US military general medical officers in FY05, NMRCDC implemented the first outbreak investigation course for general medical officers at the Peruvian National Naval Medical Center in December 2005. The GEIS optimization of video-teleconference capability allowed distance learning within and outside Peru, including clinical tropical medicine and epidemiology training. GEIS continues to support other courses, such as biostatistics, bioethics, and the Military Tropical Medicine Course sponsored by the Navy Medicine Manpower Personnel Training and Education Command (Bethesda, MD). In addition, the premier NMRCDC 5-day outbreak course was

translated into English, and both versions are posted on its website to be used freely by GEIS partners.

Electronic surveillance programs have addressed the GEIS goals and include Alerta DISAMAR for transmissible disease and outbreak notification and EWORS for timely outbreak detection. The Alerta system expanded within the Peruvian Army and was optimized in the Peruvian Navy, in which all ships are now under surveillance, and continues to detect numerous outbreaks of infectious disease. These efforts have led to timely awareness within the Peruvian Navy of disease outbreaks and enhanced cooperation between Peruvian Navy health services and NMRCDC. Additionally, baseline levels of disease have been established for many regions within Peru. These data have not existed in the past. EWORS was expanded in Peru as well, with two sites reporting from Tumbes (northern Peru) and seven sites from Lima.

## Armed Forces Research Institute of Medical Sciences *Bangkok, Thailand*

During FY06, GEIS work at the Armed Forces Research Institute of Medical Sciences (AFRIMS) expanded rapidly in programs and geography. This work built on excellent longstanding relationships with the Royal Thai Army, which hosts AFRIMS, and civilian hospitals. Much growth was driven by the supplemental funding for pandemic and avian influenza. Other GEIS work encompasses anti-malarial drug resistance surveillance, enteric illness etiology and sensitivity determination, encephalitic and febrile illness characterization, institutional laboratory and human capacity building, and international collaboration building. These programs support the four GEIS goals and provide the host nations, PACOM, and the DoD with actionable, timely surveillance data on a wide range of infectious diseases that threaten civilian and military populations alike.

Through the GEIS influenza surveillance project, rapid diagnostic kits and specimen collection and transportation capabilities are available to practitioners within the AFRIMS network. In Nepal, the Philippines, and Thailand, AFRIMS has developed and maintained at least one laboratory that can

perform PCR diagnostics. Confirmatory testing and further characterization were accomplished at the AFRIMS central respiratory laboratory facilities in Bangkok. All samples were shipped to the AFIOH, where further molecular characterization was undertaken, after which selected samples were sent to the WHO Collaborating Centre at the CDC. These capabilities show the integrated worldwide system for influenza surveillance within DoD that GEIS supports. This system provides on-site, clinically relevant information, in-country diagnostic testing for host nation action; confirmatory testing within the region, inclusion in the DoD influenza surveillance and WHO FluNet programs, and the capability for unique influenza strain acquisition for inclusion in seasonal influenza vaccines.

Current GEIS influenza surveillance projects at AFRIMS include 1) reference testing for the National Public Health Laboratory, 2) outbreak investigation in Nepal, and 3) surveillance at the US embassies in Bangladesh, Burma, China, India, Lao PDR, Malaysia, Mongolia, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, and Vietnam. In FY06, these projects yielded 490 respiratory

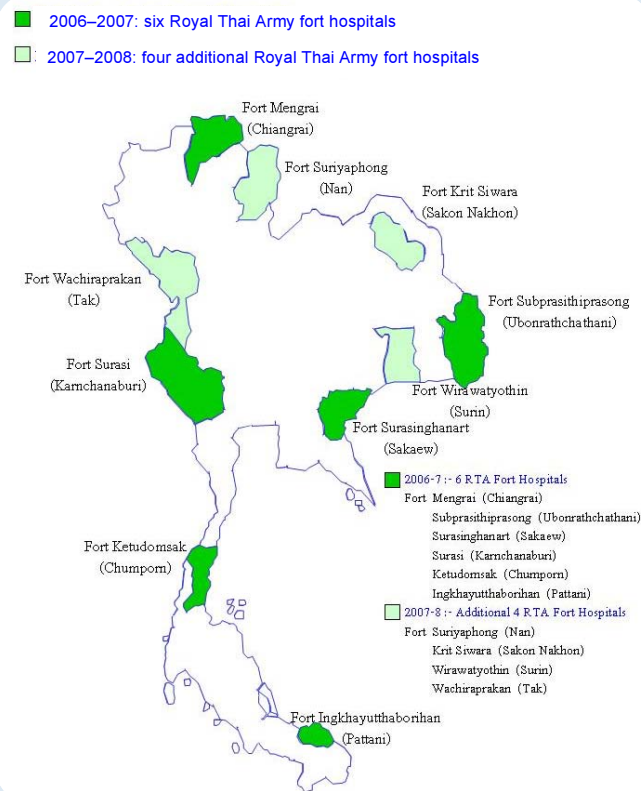
## Royal Thai Army Conducts Infectious Disease Surveillance

Securing border areas against external and internal threats is a vital mission of the Thai military. In support of this mission, Royal Thai Army units are assigned to areas near borders with Lao PDR, Cambodia, and Burma. Public health resources and communications are limited in these places, which makes timely epidemic detection and control among Royal Thai Army forces and local populations difficult, especially because many of these areas are inaccessible to the Thai Ministry of Public Health.

AFRIMS collaborators, supported by the Royal Thai Army and GEIS, developed a unit-based surveillance system in 2002 to rapidly detect and respond to disease outbreaks in military areas of operation along the Thai-Cambodian and Thai-Lao borders. The system facilitates collection of health data by individuals without medical training (e.g., Royal Thai Army soldiers). Data analysis and interpretation are then performed by medical officers in Bangkok. The US Army component of AFRIMS contributes database development and management expertise, and the Royal Thai Army component collects, analyzes, and responds to the data collected.

Each day, military units participating in the unit-based surveillance system collect syndromic information on populations residing in or transiting through their area of operation and relay syndrome counts to higher headquarters by military radio or fax (surveillance includes constitutional, respiratory, and gastrointestinal syndromes). At higher headquarters, data are transmitted through a web-based system to the AFRIMS mainframe at least twice per week. If analysis at AFRIMS identifies a possible outbreak, Royal Thai Army medical and Ministry of Public Health authorities are notified.

This system is not static. For example, sites for influenza surveillance by the Royal Thai Army are increasing. In response to outbreaks of avian influenza in Thailand in 2006, this system was updated to capture information on poultry exposure among patients with respiratory illnesses. AFRIMS has ensured that these data are integrated into the Ministry of Public Health national surveillance system, allowing access by civil health authorities to these critical data from military areas of operation.



Current and proposed Royal Thai Army influenza surveillance sites.

samples from 13 sites in five countries. GEIS-supported efforts have provided early warning of the spread of new influenza A variants. Specifically, an isolate obtained from the Walter Reed AFRIMS Research Unit-Nepal (WARUN) was found to be highly related to the influenza A/California strain months before the strain was detected in the United States.

Through GEIS support to AFRIMS, a web-based reporting system was created for suspected human or animal avian influenza cases in 18 provinces in Thailand. An example of cooperation and capacity building for the region, this system will eventually merge with another AFRIMS-supported project linking the Ministry of Public Health and Ministry of Agriculture and Cooperatives to allow sharing of



data on zoonotic illnesses among ministries at the provincial and national levels. AFRIMS also supports the Royal Thai Army surveillance programs in Thailand's border regions, a program that now includes reporting of influenza-like illness.

AFRIMS is instituting active influenza surveillance throughout Nepal, in the Philippines, in Kamphaeng Phet in Thailand, on the Burmese border with Thailand, and at six Royal Thai Army hospitals with significant cross-border traffic. Finally, the Departments of Virology and Veterinary Medicine will collaborate with the Thai Ministry of Public Health and Ministry of Agriculture and Cooperatives to study human-animal influenza transmission.

The AFRIMS Department of Immunology conducts surveillance for antimalarial drug resistance to provide timely data on current patterns of resistance to antimalarials. One recent GEIS-AFRIMS project is determining antimalarial resistance of *Plasmodium falciparum* infections in Bangladesh using a combination of in vitro and in vivo data.

Resistance to almost all classes of antimalarial drugs has been described, which undoubtedly increases the worldwide malaria burden and risk. The only class of antimalarial drugs yet to have resistance confirmed is artemisinin, of which artesunate is the most frequently used drug. Were artemisinin resistance to be confirmed, the global malaria treatment picture would be at grave risk because no effective and affordable alternatives are available. Consequently, in response to troubling reports of artemisinin failures on the Thai-Cambodian border, AFRIMS undertook comprehensive surveillance of artemisinin efficacy in this region. In a report for the 2006 American Society of Tropical Medicine and Hygiene meeting, AFRIMS and Thai Ministry of Public Health investigators presented data demonstrating 7% early treatment failures and 27% late treatment failures in vivo to the treatment combination of artesunate and mefloquine that is recommended by the Thai Ministry of Public Health. AFRIMS commenced a similar study on the Cambodian side of the border in October 2006 to identify potential areas of malarial drug resistance in that country.

The Department of Enterics has a long history of providing diarrheal illness etiology and antimicrobial susceptibility surveillance in Asia. In the past year, AFRIMS concluded a 2-year case-control study of pediatric diarrheal illness among children in Phnom Penh, Cambodia, that provided valuable current information on etiology and susceptibility in this region. A multiyear case-control study among pediatric populations in Thailand is ongoing, and results are being prepared for publication. In this study, pathogens are frequently isolated from asymptomatic controls, an important attribute of this study design. Similar studies in adult and pediatric populations are to be undertaken in Nepal and the Maldives next year.

The Department of Virology performed surveillance for etiologic agents of dengue-like syndrome and acute encephalitis syndrome in Manila. A total of 210 patients were enrolled in these surveillance activities; 143 patients underwent laboratory testing for dengue infection, of which 90% were confirmed positive. All acute encephalitis syndrome patients underwent testing for Japanese encephalitis, and 31% were confirmed positive. Among the 14 patients with dengue-like syndrome who were later confirmed as nondengue cases, the following diagnoses were made: two possible leptospirosis, one typhoid fever, one *P. falciparum*, one chikungunya, one disseminated tuberculosis, and one possible rickettsia. Further characterization of these samples, expansion of the program to Cebu, Philippines, and publication of the data are expected in the upcoming year. AFRIMS is also expanding its ability to perform febrile and encephalitic illness surveillance in Nepal, which will greatly increase capabilities for febrile illness etiology surveillance within the region.

For the third consecutive year, WARUN was called upon to investigate an outbreak of influenza-like illness among Bhutanese refugees in Nepal. WARUN also investigated a second influenza-like illness outbreak in Bharatpur, Nepal. Both of these outbreaks were caused by influenza A/H3N2. Influenza A/H3N2 strains are of particular concern because of the association of this subtype with the 1968 Hong Kong pandemic. With its location and capabilities, the WARUN laboratory is a critical component of the GEIS-supported influenza

surveillance network. In previous years, influenza A isolates from WARUN have been predictors of strains with enhanced virulence that arrived later in the United States.

The Department of Virology assisted in the laboratory diagnosis of several outbreaks of febrile illnesses, including a dengue outbreak in Timor-Leste, a dengue outbreak in the Maldives, and encephalitic and hepatic illnesses in Nepal. The Department of Medicine is completing its work on determining the impact of the 2004 tsunami on malaria in coastal Thailand as part of the GEIS-AFRIMS response to that disaster.

Laboratory capacity was expanded considerably at AFRIMS over the past year. The largest development was the preparation to build a critically needed BSL-3 laboratory, which was made possible through the supplemental funding for pandemic and avian influenza. The addition of this facility will significantly expand the capabilities of AFRIMS and other researchers to work with highly pathogenic organisms, such as select avian influenza strains. At the veterinary BSL-3 facility in Bangkok, which cannot handle the virulent organisms that will be processed by the new human BSL-3 laboratory, GEIS added real-time PCR capability to greatly enhance the possible scope of zoonotic illness surveillance programs at AFRIMS.

Through GEIS, AFRIMS continued the development of WARUN from a specimen-shipment facility to a fully functional infectious disease surveillance laboratory with the addition of ELISA, real-time PCR, and microbiology capabilities, creating the most capable laboratory, civilian or military, in Nepal. AFRIMS has additionally provided diagnostics and training to the Nepalese National Public Health Laboratory, enabling it to perform reliable Japanese encephalitis virus diagnostics in support of its national Japanese encephalitis surveillance program

AFRIMS developed the laboratory and personnel capabilities to perform febrile illness and encephalitis diagnostics in Manila and is bringing real-time PCR capabilities to its laboratory facilities in Cebu, all of which greatly enhance the reach of DoD surveillance in this critical region and support PACOM.

Training remains a cornerstone of GEIS programs at AFRIMS. In the past year, AFRIMS staff members have served as faculty for CDC and WHO regional training programs for laboratory diagnosis of avian influenza and for the rapid responder training for avian influenza response. AFRIMS hosted an epidemiology training course, taught by USUHS staff, for Ministry of Health personnel from nine countries. AFRIMS additionally provided training on avian influenza response to the Nepalese Army medical department in Kathmandu. Through GEIS, AFRIMS provided the administrative support for the Defense Threat Reduction Agency program through which numerous scientists from former Soviet nations received training in advanced medical microbiologic technologies. Finally, AFRIMS continued to serve as a training site for US military and civilian medical students, residents, and infectious disease fellows pursuing careers in tropical medicine and research.

The GEIS influenza surveillance program at AFRIMS supplies on-site rapid diagnostic kits for provider and patient benefit. Respiratory samples are then shipped to an AFRIMS in-country laboratory where real-time PCR is performed for universal influenza, influenza A, influenza B, and H5. Samples are next shipped to AFRIMS in Bangkok where results are confirmed, and further testing for H1 and H3 is performed. From AFRIMS in Bangkok, samples are then transferred to AFIOH where results are confirmed, and further characterization and testing for other respiratory pathogens are performed. The identification of various respiratory viruses by AFRIMS during FY06 is shown in Figure 14.

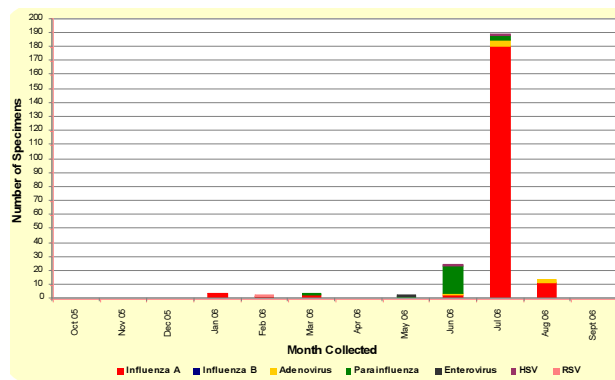


Figure 14. Number and variety of viruses found in human specimens collected during GEIS influenza surveillance at AFRIMS, 2005–2006.

### *Success in Unique Field Site Development: Walter Reed/AFRIMS Research Unit-Nepal*



A new overseas surveillance post for GEIS, Walter Reed/AFRIMS Research Unit-Nepal, in Kathmandu, Nepal.

Established in 1987 to investigate the etiology of non-A non-B hepatitis in Nepal, the AFRIMS field station in Kathmandu, Nepal, has undergone a remarkable transformation since 2005. With GEIS encouragement and support, this former specimen shipment facility has become Walter Reed/AFRIMS Research Unit-Nepal (WARUN), a fully functional laboratory for infectious disease work.

Nepal, a country of 23.1 million people located between China and India with an altitude ranging from 60 to 8,848 meters above sea level and widely divergent ecologies, is home to innumerable infectious diseases and has limited

public health laboratory capacity. In January 2005, with the hepatitis E vaccine trials closing, AFRIMS transferred administrative and scientific control of WARUN to GEIS with the intent of creating a laboratory in a region that represents the frontier of infectious disease surveillance and research in southern Asia.

Since then, WARUN has grown from a data entry and specimen processing station to an infectious disease laboratory platform. The addition of microbiology capabilities, an ELISA laboratory, and real-time PCR in FY06 has made WARUN the most advanced laboratory in Nepal.

Despite an ongoing Maoist insurrection and the abdication of the monarch brought about by street protests, all in FY06, WARUN thrived, contributing essential work in influenza and encephalitis investigations. In recognition of WARUN's continued work during the political unrest, even in the face of an evacuation of the US Embassy in Kathmandu, the US Embassy in Bangkok presented WARUN with a group Meritorious Honor Award in FY06.

With the backing of AFRIMS, WARUN now stands as the reference laboratory for the Japanese encephalitis and influenza surveillance programs of the Nepal National Public Health Laboratory. In addition, WARUN is the laboratory partner of choice for Nepalese national authorities investigating outbreaks of encephalitis, hepatitis, and influenza throughout Nepal. Through GEIS, AFRIMS continues to train laboratory and disease control personnel at WARUN and AFRIMS, ensuring that host nation development is not supplanted by the establishment of this DoD resource and to assure continued collaboration with host nation institutions.

In FY07, AFRIMS will be performing a full range of surveillance projects from WARUN, including diarrhea etiology and antimicrobial resistance, influenza, encephalitis etiology, and febrile illness etiology, to fully utilize this new and unique resource in an area from which little medical threat information is otherwise available. US and DoD infectious disease situational awareness is enhanced through the

## United States Army Medical Research Unit-Kenya

### Nairobi, Kenya

The United States Army Medical Research Unit-Kenya (USAMRU-K) devoted much effort in FY06 toward establishing and managing a national influenza surveillance program in Kenya. Other conditions for which GEIS supported surveillance included arbovirus illness, malaria drug sensitivity, and acute febrile illness.

### Surveillance

In collaboration with the Kenya Ministry of Health, the Kenya Medical Research Institute (KEMRI), and the CDC International Emerging Infections Program in Kenya, GEIS and USAMRU-K have led the development of a national influenza surveillance network in Kenya (Figure 15). This network makes Kenya is the largest sub-Saharan country with an ongoing human influenza surveillance system.



Figure 15. USAMRU-K influenza sentinel surveillance sites established in key areas during FY06: Malindi District Hospital, southeastern coast; Isiolo District Hospital, central Kenya; Port Reitz District Hospital, Mombasa; Mbagathi District Hospital, Nairobi; Kondele Children's Hospital, Kisumu/Lake Victoria region.

USAMRU-K surveillance laboratory work is conducted within the Kenya National Influenza Center (Kenyatta Hospital, Nairobi), which USAMRU-K completely renovated and equipped in FY06; the initial three surveillance sites were activated in Nairobi, Kisumu, and Malindi. Within the first 3 months (July–September) of surveillance, 258 samples were collected and sent to the National Influenza Center laboratory for analysis. Fourteen viruses (13 influenza viruses and 1 adenovirus) were isolated and partially characterized. Most influenza viruses were B/Malaysia/2506/2004-like,

whereas two were A/New York/55/2004-like (H3N2). Genotyping and molecular characterization of the present and future influenza isolates will indicate whether antigenic drifts have occurred from known strains to account for the frequent acute upper respiratory infections in Kenya.

Mosquito- and tick-targeted arbovirus surveillance forms an integral part of the GEIS febrile illness surveillance program. This type of surveillance provides the earliest evidence of transmission in an area, identifies the potential risk to humans, and allows emergency control operations to be activated well in advance of epidemics. GEIS is determining the genetic diversity, evolutionary trends, and spatial distribution of arboviruses circulating in Kenya, and evaluating the role of mosquito, sandfly, and tick species in the maintenance, transmission, and dissemination of relevant arboviruses. Vector collection was performed in FY06 at four study sites covering coastal, western, and central Kenya. Standard mosquito and tick collection methods were used, and insect species identification was performed in the field. Samples were pooled and RT-PCR and virus culture/isolation performed. More than 18,000 mosquitoes and 10,600 ticks from the surveillance sites were collected. Laboratory analysis of these samples is ongoing: Flavivirus has been detected in an *Aedes* mosquito pool from western Kenya and in a tick pool from Isiolo in northeast of Nairobi. Viral characterization to date is incomplete.

Sample collection from five sites (Kisumu, Isiolo, Malindi, Busia, and Mumias) for malaria drug resistance ceased in early FY06 in preparation for relocation of the antimalarial drug resistance laboratory from Nairobi to Kisumu (to leverage existing USAMRU-K malaria infrastructure and expertise already based in Kisumu). Laboratory analysis of the previously collected isolates comparing anti-malarial drug sensitivity patterns with quantity and types of codon mutations in the *Plasmodium* parasites was completed. An increase in pyrimethamine/sulfadoxine resistance was observed. However, an encouraging sharp decrease in chloroquine resistance at all study sites was observed, presumably because of decreased drug



pressure as Kenya switched from chloroquine to other antimalarials when chloroquine resistance became widespread.

The acute febrile illness protocol, which was originally designed for inpatient yellow fever-type illness surveillance, saw quality improvements in case identification, data collection, sampling, transport, and laboratory analysis. In FY06, seven samples from Kisumu were positive for West Nile virus, and one sample from Malindi was positive for chikungunya virus by immunoglobulin M ELISA. A new protocol is being written that will focus more generally on cases of fevers of unknown origin.

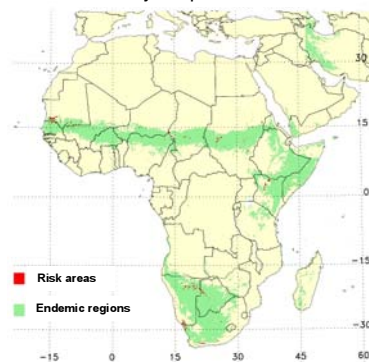
The USAMRU-K GEIS program also participated in joint avian influenza surveillance with NAMRU-3, CDC-Kenya, and the Kenya National Museum. From October 2005 to March 2006, 367 migratory birds were caught, registered, and sampled. Influenza A virus was found in 24 (15.3%) birds. Four samples tested positive for H5 hemagglutinin but were not of the highly pathogenic H5N1 subtype. This surveillance is important because Kenya is part of the migratory bird flyway that connects Africa with Europe and western Asia.

Conducting surveillance for Rift Valley fever has always been a GEIS priority at USAMRU-K, particularly given the proximity of USAMRU-K to the Great Rift Valley, where the virus was first seen. GEIS supports NASA satellite-based surveillance for environmental conditions that favor Rift Valley fever epidemics. Monthly risk predictions are publicly available on the GEIS website.

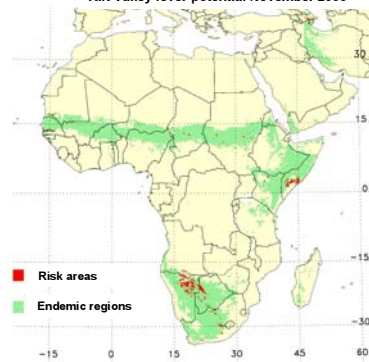
In December 2006, a fatal outbreak of Rift Valley fever occurred in northern Kenya. The outbreak, which was severe enough for WHO to initiate a response through the Global Outbreak Alert & Response Network, was predicted by the NASA-GEIS work during FY06. In November, NASA and GEIS notified USAMRU-K of the likelihood of an outbreak of Rift Valley fever in areas targeted by the modeling. USAMRU-K communicated with public health authorities in Kenya and began collecting mosquito specimens near areas that later were affected. The accuracy of the NASA prediction improved situational awareness and allowed public health officials to pinpoint locations for surveillance efforts more than a month in advance of the outbreak.

## Satellite Data Predict Rift Valley Fever Outbreak

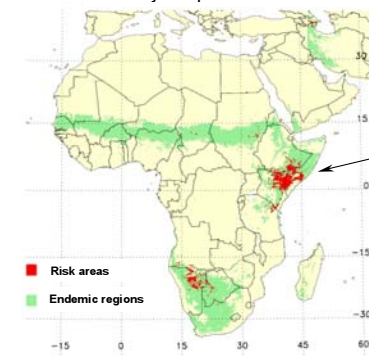
Rift Valley fever potential October 2006



Rift Valley fever potential November 2006



Rift Valley fever potential December 2006



Area where fatal outbreak of Rift Valley fever occurred in December 2006

The GEIS-sponsored NASA remote sensing program predicted high risk of a Rift Valley fever epidemic in East Africa 2 months before the outbreak was identified in eastern Kenya in late 2006. Through this collaboration, satellite-derived climate data such as sea surface temperature, outgoing longwave radiation, and normalized difference vegetation index (NDVI) are used to forecast where certain vector-borne diseases might occur in Africa and on the Arabian peninsula. In these images, regions where Rift Valley fever is endemic (*green*) and regions that have experienced persistent heavy rainfall as measured by NDVI (*red*) indicate areas of potential risk for Rift Valley fever transmission.

## Response

USAMRU-K investigated an influenza-like-illness outbreak in Kombewa near Lake Victoria in June and July 2006. Specimens were collected and characterized as influenza B/Florida/07/2004-like. This virus is a B/Yamagata lineage virus similar to the 2005 Southern Hemisphere and the 2006 Northern Hemisphere vaccine strains. However, it is not similar to the 2006 Southern Hemisphere strain of influenza B, and this may explain the ineffectiveness of the current vaccine to control illness caused by this virus.

USAMRU-K also upheld its regional epidemic response mission by supporting the work of the WHO regional arbovirology and viral hemorrhagic fever reference laboratory for East Africa, which is housed at KEMRI. Eighty-seven samples were analyzed from 17 sites including Sudan and the Congo. Eight specimens from Comoros tested positive for chikungunya virus. Most were negative for arboviruses or viral hemorrhagic fever, although some were positive for measles or hepatitis E, demonstrating that these diseases still circulate in the region.

## Integration

GEIS surveillance programs use a network of clinical centers across Kenya. Four sites (Kisumu, Malindi, Isiolo, and Busia) were maintained, and one site (Mumias) was closed. Influenza-like illness and diarrheal specimen collection began at a new site, Mbagathi District Hospital in Nairobi, during FY06. This hospital site is significant because it

primarily serves the Kibera slum, one of the largest slums in Sub-Saharan Africa, so the collections will identify infections in an underserved, poor population that carries a high burden of disease and might otherwise not be represented in surveillance based on care in clinics.

The collaboration between the GEIS program at USAMRU-K and the CDC-Kenya to cooperatively build the Kenyan influenza surveillance network has required flexibility and effective communication. Sharing of knowledge, resources, and existing surveillance assets has resulted in increased capacity and response capability and should be the model for future surveillance activities in Africa. Discussions are already underway to combine future efforts and expertise in arbovirus surveillance.

## Capacity Building

Two USAMRU-K technicians from the enterics laboratory participated in a 3-week practical laboratory training program sponsored by GEIS at NAMRU-3 in Cairo in August 2006. USAMRU-K also participated in a training course to teach the skills essential to human and bird influenza surveillance to participants from Kenya, Uganda, Cameroon, and Burundi that was held in May 2006 at the KEMRI training center in Nairobi. The training, which was both theoretical and practical, covered topics including influenza virology, case finding, epidemiology, quality assurance and control, specimen collection, laboratory diagnostics, and safety. USAMRU-K also helped support and operate the GEIS-funded malaria microscopy diagnostic center of excellence that operates in Kisumu.

## National Aeronautics and Space Administration

Raw data on climate conditions are routinely collected by National Aeronautics and Space Administration (NASA) satellites and form the basis for GEIS infectious disease modeling to predict specific locations throughout the world for outbreaks of selected diseases. This ongoing work is included in this section because it involves collaboration with several DoD overseas laboratories.

### Global Climate Anomalies and Potential Disease Risks

The Global Inventory Mapping and Monitoring System group at the NASA Goddard Space Flight Center (Greenbelt, MD) produces and compiles long time series measurements of vegetation and rainfall for Africa and the Saudi Arabian peninsula and compiles global sea surface temperature and

outgoing longwave radiation. Created from data collected by NASA satellites, these data sets are used to monitor climatic conditions through anomaly analyses associated with epidemics and to map regions at risk for outbreaks of Rift Valley fever and other vector-borne diseases.

Identification and mapping of risk areas involve tracking and computation of a persistence index of above-normal vegetation conditions associated with above-normal rainfall. Global scale indicators of interannual climate variability such as El Niño/Southern Oscillation are monitored to provide guidance on areas that could be affected by extreme climatic events, such as floods or drought, with an impact on vector population emergence and dynamics. With GEIS funding, NASA provided detailed analyses of satellite vegetation and related derived global climate data sets (including sea surface temperature and outgoing longwave radiation and rainfall) to support the GEIS monitoring of climatic conditions and ecological dynamics associated with Rift Valley fever outbreaks in Africa and the Saudi Arabian peninsula. These general analyses of global climate conditions also provide on-demand information products for other GEIS vector-borne disease monitoring activities worldwide.

The National Oceanic and Atmospheric Administration issued an unscheduled El Niño conditions advisory in late 2006. El Niño/Southern Oscillation is the most well-known phenomenon influencing the global climate variability at interannual time scales. The term El Niño refers to the large-scale ocean-atmosphere climate phenomenon linked to a periodic warming in sea surface temperatures across the central and east-central equatorial Pacific, between approximately the date line and 120° west. El Niño represents the warm phase of the El Niño/Southern Oscillation cycle and is sometimes referred to as a Pacific warm episode. (El Niño originally referred to an annual warming of sea surface temperatures along the west coast of tropical South America). Given the large size of the Pacific Ocean, changes in the sea surface temperature patterns and gradients across the basin influence atmospheric circulation with pronounced impact on global tropical precipitation patterns and therefore potential numbers of insect vectors in areas endemic for infectious disease. Accordingly, El Niño may alter the risk for disease in these areas.

## Hotspots of Potential Disease Outbreaks

The development of El Niño conditions has significant implications for global public health. The dramatic displacements in large-scale precipitation centers around the global tropics will likely lead to extremes in climate events with above-normal rainfall and flooding in some regions and extended drought periods in other regions. These extremes will likely affect vector abundance in different ways, many of which can elevate the risk of infectious disease outbreak. Drought conditions can suppress predators, whereas heavy rains will boost food supplies—a synergy that can, for example, spark rodent population explosions and create appropriate conditions for mosquito breeding and propagation. The likelihood is high through most of 2007 for drought conditions to prevail over southeast Asia, Mexico, northeast Brazil, and southern Africa and for above-normal rainfall and flood conditions to occur over coastal Peru, southern California, the US Gulf Coast and Florida, and eastern Africa. Previous El Niño events have been associated with disease outbreaks and with spatial clusters of mosquito-, water-, and rodent-borne illnesses. Given current FY06 observations and forecast information, the following regions are at increased risk for disease outbreak (Figure 16).

- Indonesia, Malaysia, Thailand, and most islands of southeast Asia: 1) increased dengue fever transmission caused by drought conditions that increase water storage around houses (which lead to elevated *Aedes aegypti* populations) and elevate ambient air temperatures (which reduce the extrinsic incubation period for the dengue virus in vector mosquitoes, increasing vector capacity) and 2) respiratory illness caused by particulate-laden haze from uncontrolled burning of tropical forests that accompanies extreme drought.
- Coastal Peru, Venezuela, and Colombia: malaria caused by elevated *Anopheles* vector populations that will develop when various immature habitats are flooded after heavy rainfall.
- Bangladesh and coastal India: cholera.
- East Africa (Kenya, Somalia, and Ethiopia): Rift Valley fever and malaria resulting from elevated mosquito vector populations and cholera caused by flooding after heavy rainfall in dry land areas. This Rift Valley fever prediction proved accurate when a fatal outbreak began in northern Kenya in December 2006 .



- Southwestern United States (New Mexico and Arizona): hantavirus pulmonary syndrome and plague caused by elevated rodent populations that develop after heavy rainfall.
- Southern California: increased potential for transmission of arboviruses, such as West Nile virus, associated with elevated *Culex* species mosquito populations resulting from the heavy rainfall.
- Northeast Brazil: dengue fever and respiratory illness caused by drought conditions and accompanying large-scale forest fires.



Figure 16. Areas predicted to be at elevated risk for infectious disease outbreaks by NASA-GEIS FY06 remote sensing modeling based on 2006–2007 El Niño conditions. The area over Africa was the site of the December 2006 Rift Valley fever outbreak, demonstrating the utility of the model. CHOL, cholera; DENG, dengue fever; HPS, Hantavirus pulmonary syndrome; MAL, malaria; PL, plague; RI, respiratory illness; RVF, Rift Valley fever.

### Use of NASA-GEIS Information

Output data from this project are provided as 1) early warning satellite vegetation index and rainfall products to NAMRU-3 in Cairo, WHO, and the Food and Agriculture Organization of the United

Nations in collaboration with the Yemen and Saudi Arabia ministries of health and ministries of agriculture as an alert to conduct field investigations in regions at risk for Rift Valley fever and 2) risk maps to NAMRU-3 identifying areas of yellow fever outbreaks in Sudan. NASA also provided USAMRU-K and GEIS, in collaboration with CDC and WHO, vegetation index anomaly maps, sea surface temperature, and outgoing longwave radiation data in support of field surveillance investigation during the large-scale chikungunya outbreak along the East African coast and islands in the western Indian Ocean. Additionally, monthly electronic reports on Rift Valley fever monitoring are provided to WHO and the Food and Agriculture Organization of the United Nations in support of continental efforts to monitor and suppress Rift Valley fever activity. Finally, NASA publishes monthly Rift Valley fever risk maps for continental Africa, Madagascar, and the Saudi Arabian peninsula for global public dissemination through the GEIS Headquarters website (<http://www.geis.fhp.osd.mil/GEIS/SurveillanceActivities/RVFWeb/indexRVF.asp>).

The GEIS remote sensing project through NASA has helped foster and support field investigations with USAMRU-K in collaboration with the USDA Agricultural Research Service on mosquito vector ecology and identification of potential sites for testing of mosquito control measures currently under development. Such specific field projects help test, validate, and improve the epidemic prediction models.



## Appendix:

### Countries with GEIS Activities in FY06

Afghanistan	Indonesia	Palestine
Argentina	Iraq	Paraguay
Armenia	Iran	Peru
Azerbaijan	Italy	Philippines
Bangladesh	Japan	Qatar
Bolivia	Jordan	Republic of Georgia
Bulgaria	Kazakhstan	Romania
Burma	Korea	Saudi Arabia
Cambodia	Kuwait	Senegal
China	Kyrgyzstan	Sri Lanka
Colombia	Lao PDR	Sudan
Comoros	Libya	Syria
Congo	Macedonia	Thailand
Djibouti	Malawi	Tunisia
Ecuador	Malaysia	Turkey
Egypt	Maldives	Ukraine
El Salvador	Mexico	United Kingdom
Ethiopia	Mongolia	United States
Germany	Morocco	Uruguay
Ghana	Nepal	Uzbekistan
Guam	Nicaragua	Venezuela
Guatemala	Nigeria	Vietnam
Honduras	Oman	Yemen
India	Pakistan	

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## Posters/Presentations

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2. Alker, A.P., N. Shah, R. Sem, P. Yi, S. Nemh, P. Lim, D. Mey Bouth, R. Tsuyuoka, J.D. Maguire, F. Arie, T. Fandeur, C. Wongsrichanalai, and S.R. Meshnick. The association between Pfm1r copy number and clinical outcome of artesunate-mefloquine therapy for Plasmodium falciparum malaria in Pailin, Cambodia. Presented at the American Society of Tropical Medicine and Hygiene Annual Meeting, 2005 Dec; Washington D.C.
3. Anyamba, A., J.P. Chrétien, J. Small, C.J. Tucker, J.L. Malone, and K.J. Linthicum. Potential for Rift Valley Fever Expansion: Eco-climatic Conditions on the Arabian Peninsula. Presented at the SOVE 4th International Congress of Vector Ecology; 2005 Oct; Reno, NV.
4. Anyamba, A., J.P. Chrétien, S. Yingst, J. Small, K.J. Linthicum, and C.J. Tucker. Satellite-Based Rift Valley Fever Forecasts Predict a Large Yellow Fever Epidemic in Sudan, 2005. Presented at the International Conference on Emerging Infectious Diseases; 2006 March; Atlanta, GA.
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33. Felices, V., C. Cruz, V.A. Laguna-Torres, L. Beingolea, C. Naquira, V. Suarez, L. Suarez, G. Jave, G. Chauca, T. Kochel, and J.G. Olson. Dengue-3 in Lima, Peru, 2005. Presented at the American Society of Tropical Medicine and Hygiene 54th Annual Meeting, 2005 Dec; Washington, D.C.
34. Flores, C., F. Chapilliquen, L. Cubillas, P. Villaseca, W. Leon, L. Campos, F. Castro, J. Perez, and J. Stancil. Distribution of *Aedes aegypti* in three districts of Lima, Peru. Presented at the American Society of Tropical Medicine and Hygiene Annual Meeting, 2005 Dec; Washington, D.C.
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37. Gaydos, J.C. Emergence of a Possible Pandemic Influenza Virus on a Military Installation - Investigation of the 1976 Swine Influenza Outbreak. Presented at the Fifth Annual Syndromic Surveillance Conference, 2006 Oct; Baltimore, MD.
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42. Glass, J.S. The Re-emergence of Chikungunya Virus in Indonesia.. Presented at the American Society of Tropical Medicine and Hygiene Annual Meeting, 2005 Dec; Washington D.C.

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44. Graf, P.C.F., J.P. Chrétien, L. Ung, J.C. Gaydos, and A.L. Richards. *Anaplasma phagocytophilum* and *Rickettsia rickettsii* Seroprevalence in US Military Personnel. Presented at the 44th Annual Meeting of the Infectious Diseases Society of America, 2006 Oct; Toronto, Ontario, Canada.
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63. Kajon, A.E., J.M. Moseley, A. Wadleigh, D. Metzgar, and K.L. Russell. Molecular epidemiology of adenovirus 4 infections of U.S. military recruits between 1997 and 2003. Evolutionary trends after elimination of vaccine selective pressure. Presented at the 8th International Adenovirus Meeting, 2006 Aug-Sep; Zurich, Switzerland.
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## Acronyms

AFEB	Armed Forces Epidemiological Board	DoD	Department of Defense
AFHSC	Armed Forces Health Surveillance Center	DoDVSA	DoD Veterinary Service Activity
AFIOH	Air Force Institute for Operational Health	ELISA	enzyme-linked immunosorbent assay
AFIP	Armed Forces Institute of Pathology	EOC	emergency operations center
AFMETS	Armed Forces Medical Examiner Tracking System	Epi-X	Epidemic Information Exchange
AFMIC	Armed Forces Medical Intelligence Center	EPICON	epidemiology consultation
AFRIMS	Armed Forces Research Institute of Medical Sciences (Bangkok, Thailand)	ESBL	extended-spectrum beta-lactamase
AIDS	acquired immune deficiency syndrome	ESSENCE	Electronic Surveillance System for the Early Notification of Community-Based Epidemics
ARDS	acute respiratory distress	EUCOM	European Command
BAMC	Brooke Army Medical Center	EWORS	Early Warning Outbreak Recognition System
BSL	biosafety level	FDA	Food and Drug Administration
CA-MRSA	community-acquired methicillin-resistant <i>Staphylococcus aureus</i>	FRI	febrile respiratory illness
CDC	Centers for Disease Control and Prevention	FY	fiscal year
CDHAM	Center for Disaster and Humanitarian Assistance Medicine	G6PD	glucose-6-phosphate dehydrogenase
CENTCOM	Central Command	GEIS	Global Emerging Infections Surveillance and Response System
CGTC	Coast Guard Training Center	GPS	global positioning system
CHCS	Composite Health Care System	HHS	Department of Health and Human Services
CHPPM	see USACHPPM	HIV	human immunodeficiency virus
CHPPM-EUR	United States Army Center for Health Promotion and Preventive Medicine-Europe	HL7	Health Level Seven
CI	confidence interval	HSV	herpes simplex virus
CIS	Clinical Information Systems	ICD-9	International <i>Classification of Diseases</i> , 9th Revision
COCOM	Combatant Command	IFA	immunofluorescence assay
CONUS	continental United States	KEMRI	Kenya Medical Research Institute
CY	calendar year	JHU/APL	Johns Hopkins University Applied Physics Laboratory
DNBI	disease nonbattle injury	JMEWS	Joint Medical Workstation
		JPTA	Joint Patient Tracking Application
		JTF-Bravo	Joint Task Force Bravo
		LRMC	Landstuhl Regional Medical Center



MCRD	Marine Corps Recruit Depot	RSV	respiratory syncytial virus
MEDCOM	Medical Command	RT-PCR	reverse transcriptase-polymerase chain reaction
MHS	Military Health System	RTA	Royal Thai Army
MLST	multilocus sequence typing	SADR	Standard Ambulatory Data Registry
MOH	Ministry of Health	SARS	severe acute respiratory distress syndrome
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>	SIDR	standard inpatient data records
MTF	military treatment facility	SOUTHCOM	Southern Command
NAMRU-2	Naval Medical Research Unit No. 2 (Jakarta, Indonesia)	SSN	social security number
NAMRU-3	Naval Medical Research Unit No. 3 (Cairo, Egypt)	SUBPAC	Pacific Submarine Force
NASA	National Aeronautics and Space Administration	TIGER	triangulation identification for genetic evaluation of risks
NDVI	normalized difference vegetation index	TRAC <sup>2</sup> ES	TRANSCOM Regulating and Command and Control
NEHC	Navy Environmental Health Center	TRANSCOM	Transportation Command Evacuation System
NEPMU	Navy Environmental and Preventive Medicine Unit	TSN	The Surveillance Network®
NHRC	Naval Health Research Center	USACHPPM	United States Army Center for Health Promotion and Preventive Medicine
NIC	National Influenza Center	USAID	United States Agency for International Development
NIH	National Institutes of Health	USAMRIID	United States Army Medical Retute of Infectious Diseases
NMRC	Naval Medical Research Center	USAMRU-K	United States Army Medical Research Unit-Kenya
NMRC D	Naval Medical Research Center Detachment (Lima, Peru)	USARSO	United States Army, Southern Command
NORTHCOM	Northern Command	USDA	United States Department of Agriculture
NSTC	Naval Service Training Command	USFK	United States Forces Korea
OCONUS	outside the continental United States	USUHS	Uniformed Services University of the Health Sciences
ODS/S	Operation Desert Storm/Shield	WARUN	Walter Reed/AFRIMS Research Unit-Nepal
OEF	Operation Enduring Freedom	WB	Western blot
OIF	Operation Iraqi Freedom	WHO	World Health Organization
PACOM	Pacific Command	WRAIR	Walter Reed Army Institute of Research
PCR	polymerase chain reaction		
POPM	Program Office for Preventive Medicine		
RAPIDS	Ruggedized Advanced Pathogen Identification Device		
RME	reportable medical event		
ROK	Republic of Korea		



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